Medical
Wales
coll. 1

SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 88 JANUARY, 1949 NUMBER 1

APOCRINE TISSUE, CHRONIC CYSTIC MASTITIS AND SWEAT GLAND CARCINOMA OF THE BREAST

JOHN F. HIGGINSON, M.D., and JOHN R. McDONALD, M.D., Rochester, Minnesota

SINCE "pale epithelium" was first described, it has been the object of numerous pathologic and experimental studies. It has been considered variously as evidence of degeneration; carcinomatous tissue; precancerous tissue; evidence of atavism, metaplasia, heteroplasia and alloplasia; a variant of normal breast tissue; sweat gland tissue; and finally, and most important, apocrine skin gland tissue.

It has been found by some workers in the periphery of the normal breast and by fewer workers in the depths of the normal breast proper. It has been related etiologically to carcinoma of the breast and especially to chronic cystic mastitis; it has also been listed as an accompaniment of these and other lesions of the breast. Many papers have been written concerning the embryology of the breast and other cutaneous glands, especially the sweat glands, which tend to show a common origin or relationship, or none at all. Morphologic studies have been reported, clinical observations have been recorded and experiments have been performed which show a relationship of "pale epithelium" in the breast to sweat glands, to various pathologic and physiologic body states and to various hormonal imbalances.

Abridgment of thesis submitted by Dr. Higginson to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

From the Division of Surgery, Mayo Foundation, and the Section on Surgical Pathology, Mayo Clinic.

Fig. 1. Axillary specimen of skin showing apocrine glands in secretory and resting stages. The eosinophilia is apparent. Also visible are a sebaceous gland and an eccrine (true sweat) gland. Hematoxylin and eosin, ×33.

Fig. 2. Same tissue as in Figure 1. View of tall columnar epithelium which contains red-staining and brown pigment granules. Myoepithelial cells can be seen in cross section on the left and in longitudinal section above on the right. Hematoxylin and eosin, ×280.

Fig. 3. Section from a breast removed for carcinoma (malignant tissue not shown here). The pale epithelium is seen in, and as part of a lobule of, the breast surrounded by "normal" or usual mammary tissue. No cystic change is present. Hematoxylin and eosin, ×45.

Fig. 4. Section from a breast removed for extensive chronic cystic mastitis. Note cystic change in acini and papillary formation of the pale epithelium. Hematoxylin and eosin, ×17.

Fig. 5. Section from a breast removed for chronic cystic mastitis. Note the eosinophilic granules and the fewer brownish granules. Hematoxylin and eosin ×225. Compare with Figure 2.

Fig. 6. Section from a breast removed for carcinoma (malignant tissue not shown here). Note brown-yellow pigment granules (in unusual abundance in this section), and also a few fat droplets. Myoepithelial cells in tangential and longitudinal section. Hematoxylin and eosin, ×225.

Fig. 7. Section from a breast removed for carcinoma (malignant tissue not shown here). Note direct continuity between apocrine scent gland type of tissue ("pale epithelium") and usual, or "normal" mammary tissue. Hematoxylin and eosin ×130.

Fig. 8. Section from a breast removed for carcinoma (malignant tissue not shown here). "Pale epithelium" shows hyperplasia. Enlarged, hyperchromatic, nuclei contain enlarged, hyperchromatic, often multiple, nucleoli. Two, three, and four nucleoli can be seen in some instances. Hematoxylin and eosin, ×325.

Fig. 9. Section from a breast removed for carcinoma; malignant cells are visible. The morphologic and especially the staining characteristics are similar to those of "pale epithelium" except for the obvious signs of malignancy. These cells look strikingly different from those in the commoner carcinoma of breast. Hematoxylin and eosin, ×45.

The purpose of the study recorded herein was to attempt to establish the status of the so called pale epithelium in the breast.

The frequent finding of this tissue in routine sections of surgically resected breasts aroused curiosity concerning it and moreover, the term, "Schimmelbusch hyperplasia," which is used to designate this tissue, was thought, and later found, to be incorrect. In addition, the similarity of appearance of this "pale epithelium" and the epithelium of apocrine "sweat" glands elsewhere in the body seemed to indicate a relationship not commonly discussed or understood.

For the purpose of this study a review of the literature was undertaken, covering the embryology, physiology, morphology, and pathology of the cutaneous glands, particularly the mammary and other apocrine skin glands.

In addition, 97 unselected, surgically removed breasts were studied to redetermine the incidence of pale epithelium in pathologic breasts, the histologic picture presented by this tissue, and the degree of similarity in structure and staining reaction of this tissue to that of apocrine skin gland tissue such as is found in the axilla. For the latter comparison, postmortem specimens of axillary skin were obtained at random from 6 subjects, of varying sex and age; in these cases death had resulted from various illnesses but in none were there lesions of the breast. There are three types of cutaneous glands in the human being; namely, (1) the holocrine (sebaceous) glands, (2) the eccrine (sweat) glands, and (3) the apocrine glands. The last mentioned consist of odoriferous or accessory sex glands which are found in the axilla, in the groin and genital region, and in the perianal region, the ceruminous glands, Moll's glands, and the mammary glands.

Apocrine glands are not *sweat* glands in any manner, as we understand and use the term "sweat."

The preponderance of opinion is that there is a natural relation among these various types of apocrine glands on developmental, embryologic, and morphologic grounds, and this natural relationship therefore offers a logical explanation and understanding of the presence in the breast of tissue resembling, or identical with, other apocrine gland tissue such as is found in the axilla.

This study confirms those of others who have remarked on the morphologic and staining similarity and lends support to the argument that there is a logical basis for the histologic appearance of certain lesions of the breast such as the much mooted, so called sweat-gland carcinoma of the breast.

REVIEW OF LITERATURE

Robin and Horner (18, 19) emphasized sharply the difference between the 2 types of sweat glands in man and, working individually, they noted that in the axilla these glands lay in a definitely localized group, but that they also could be found in the inguinal fold. Both men noted that there seemed to be a distinct and prominent odor emitted from these glands, Horner terming them "the odoriferous glands," and both men observed that the glands were macroscopic and appeared to have a pink or reddish color. Schiefferdecker offered the following classification of the cutaneous glands:

1. Holocrine glands (sebaceous gland or hair follicle gland)

2. Merocrine glands

a. Merocrine-apocrine glands ("large sweat glands" in human beings, the glands of the hairy skin of most mammals, and the "milk glands" and "mammary glands")

b. Merocrine-eccrine glands ("small sweat glands" in human beings, the glands in the soles of the paws of the cat and the dog, in the snout of the swine, and in small numbers in the skin of some apes and so forth)

He made the point that actually the apocrine glands are not real or true cutaneous glands but an entirely special type of gland which is found in various parts of the body. In mammals these glands can and do occur in the skin and so, in these animals, they become cutaneous glands. "In this way they fortuitously become neighbors of the eccrine glands, but they have nothing whatever to do with them and form an entirely special and different group which I shall term the Stoffdrüsen or apocrine glands."

Schiefferdecker considered the Montgomery glands of the areola to be developmental links

between the "sweat" glands and the milk glands. Rein in 1882 noticed the earliest trace of the anlage of the breast in the human embryo of 24 millimeters (6 to 7 weeks old) and stated that he considered the Montgomery glands to be miniature copies of the mammae but at a slightly earlier stage of development. Benda (1, 2) considered the deeper portion of the Montgomery gland to be of the apocrine "sweat" gland type. Brouha in 1905 correlated the human areola with the peripheral section of the primitive mammalian gland field. Brouha and later Schiefferdecker stated that this fact easily explained the participation of the areolar glands in the secretion by the milk gland at the time of birth (witch's milk) and also the occasionally seen phenomenon of secretion of milk by these glands which earlier (in lower animals) were regularly employed in the nourishment of the newborn. They stated that, accordingly, in human beings there can be found in the milk glands and in the areolae all gradual changes or transitions of the apocrine glands from the central large milk gland through the smaller accessory milk glands to the usual apocrine glands.

Richter found iron in all of the apocrine glands of men and animals that he examined, and he considered its presence a general earmark. He stated also that these glands secreted cholesterin, an observation which had been made previously by Walter (50) in 1924.

Way and Memmesheimer agreed with Herzenberg and others that the apocrine glands deserve consideration as "accessory sexual glands." They stated that there seemed to be a definite relation between cellular activity and the amounts of cholesterol and hemofuscin present, and they found these substances as well as hemosiderin in their specimens.

Kölliker (21) and Talke (46, 47) were among the first to mention and describe muscular fiber cells in the sweat glands.

Sheldon in 1941 found myoepithelium present in breasts, eccrine and apocrine sweat glands, Moll's glands and the ceruminous glands of the ear. Similar contractile epithelial elements called "basket" cells are found in the salivary and lacrimal glands, as noted by Loeb. Kölliker (22) in 1889 described the myoepithelium as forming the outer of two layers of cells within the basement membrane. This myoepithelium is considered to be ectodermal in origin (Kölliker, 22, von Eggeling, Schiefferdecker, Hamperl, Sheldon, Kuzma, and others).

In 1941 Suzuki in discussing carcinoma of the sweat glands stated that one class, which he called "carcinoma sudoripara cysticum papilliferum," should include the sweat gland adenocarcinomas of the vulva, carcinomas of apocrine glands elsewhere, such as von Walko's case (ceruminous gland) and Salzmann's case (Moll's glands), and also so called sweat gland carcinomas of the breast. Gates, Warren, and Warvi stated that the histogenetic relationship had not been established between apocrine glands and the cells of some types of carcinoma of the breast, as, in their opinion, all of the cutaneous appendages, including the mammary gland derive from the primitive surface epithelium independently.

In 1937, Weiner suggested that Paget's disease of the skin is the result of intraepidermal metastasis from an underlying carcinoma of apocrine sweat glands, and he noted that the lesion in all cases of extramammary Paget's disease occurs in sites where apocrine glands are found and that mammary glands are also modified apocrine glands.

Krompecher (24) expressed the thought that small cysts lined with "pale epithelium" could be found in normal as well as in cystic and cancerous breasts; he found them in all but 1 of 23 cases of cystic disease of the breast. He offered two possible explanations for the occurrence in the breast of this "pale epithelium": (1) that genuine coiled sweat glands of the skin in the form of aberrant buds in breast tissue occurred and underwent cystic enlargement and (2) that the breasts, since they are phylogenetically derived from "sweat" glands, in the course of their development by steps, remained behind, in part, at a phylogenetically earlier stage nearer that of the "sweat" glands. He considered the latter explanation more likely because he never saw in the breast typical, quite normal, "sweat" glands, but instead saw "sweat" gland cysts which indicated to him a defective differentiation and favored an atavistic phenomenon.

In 1924 Krompecher (25) stated that the similarity between cysts of "pale epithelium" in the breast and cysts of the axillary "sweat" glands is so striking that they must be identical. He noted the unusual size of the cells, their clublike appearance when distended and their firm, occasionally granular or finely vacuolated, cytoplasm which stained yellow with van Gieson's stain and reddish with eosin.

Ewing stated that true sweat glands are not present in the breast but that in many cases there is in the breast a type of gland which we speak of as sweat glands; "I feel that this is a special form of gland structure in the breast which develops in a certain type of subject, notably those with an oily skin and many sweat glands in other parts of the body; some men think there is a transition between the ordinary acini and the sweat gland." He estimated that 25 per cent of mammary carcinomas arise from "sweat" glands distributed throughout the breast but mostly along the margins, beneath the skin and in the axillary region. He described one form of cyst in chronic cystic mastitis as developing from the "sweat" glands in the breast.

Lee, Pack, and Scharnagel agreed with von Eggeling's statement that the mammary and "sweat" glands are homologous structures which develop from a common, primitive, tubular type of epidermal gland. They stated their belief that "sweat" glands (apocrine) are normally present in every breast, where they anastomose with, and empty their secretions into, the interlobular lacteal ducts. They said it is unimportant to determine whether the "pale epithelium" is anomalous, embryonal, normal or degenerative tissue, their major premise being that the breast is a modified "sweat" gland and that the appearance of "sweat" gland tubules and cysts in the breast is a logical occurrence regardless of the mode of origin. They considered it significant that the anatomic and staining characteristics of this tissue remained throughout all the transitional phases of normal "sweat" gland tubule, cyst, intracystic papilloma, adenoma and carcinoma.

In the same year Logie reported "pale epithelium" in 60 per cent of 330 malignant and nonmalignant tumors of the breast.

In January, 1946, Foote and Stewart recognized "sweat" gland carcinoma as constituting 1 per cent of carcinomas of the breast and stated that it should properly be called "apocrine sweat gland carcinoma." They expressed the belief that the cells of the ducts or lobules undergo apocrine metaplasia, and they found convincing transitions ranging from typical apocrine epithelium, to apocrine epithelium in atypical hyperplasia, to intraductal apocrine "sweat" gland carcinoma and, finally, to infiltrating carcinoma made up of apocrine-like cells.

SCHIMMELBUSCH HYPERPLASIA

As previously noted, "pale epithelium" has been described in many pathologic specimens from the breast, especially in those which have been the seat of chronic cystic mastitis. It has been the custom at the Mayo Clinic, perhaps elsewhere also, to describe the last-mentioned specimens with the diagnostic appellation "chronic cystic mastitis with areas of Schimmelbusch hyperplasia." The latter portion of this term we consider incorrect.

Although Moullin in 1881 and Dreyfuss in 1888 had mentioned the pale structures, Schimmelbusch, if he noted such tissue at all, made no specific mention of it. Under the title "cystadenoma of the breast," in 1890 (40) and again in 1892 (41) he gave his description of what he said had been described previously by Reclus (33, 34) as *maladie kystique des mamelles*. He stated that he thought it should be called "cystadenoma," because in addition to the cyst formation there was growth or proliferation of the glandular tissue.

With hindsight it is possible to suppose that Schimmelbusch did see what we now call "pale epithelium" and that he described it as an intrinsic part of chronic cystic mastitis. However, judging from his description one can merely say that he never described "pale epithelium."

In the years that followed, other men used the term "Schimmelbusch's disease" synonymously with "cystic disease of the breast," "mastopathia cystica," or "chronic cystic mastitis," and so forth, in their descriptions and discussions of "pale epithelium." Most of these workers, in correlating the various de-

scriptions of the broad clinical and pathologic entity known most popularly as "chronic cystic mastitis," placed the phase described by Schimmelbusch at the upper, or more hyperplastic, end. This probably strengthened further the misconception concerning what Schimmelbusch saw and described (4, 6, 10, 23-25).

Cheatle and Cutler in 1931, Cutler in 1932, and Cheatle in 1935 stated that what Schimmelbusch described, they considered the neoplastic stage of cystipherous desquamative epithelial hyperplasia, and the pictures of the papillary epithelium shown by them as neoplasia are pictures of pale epithelium.

It thus may well be that Schimmelbusch actually saw what we now know as "pale epithelium." It would seem likely that he had seen it, since it is so commonly present in chronic cystic mastitis. However, we have only his descriptions from which to judge, and he does not mention pale structures or "pale epithelium," though he does mention papillary epithelial proliferations.

The use of the term "Schimmelbusch hyperplasia" at the clinic has been largely a matter of convenience and has been well understood; it was also recognized by most of the pathologists as incorrect, even before this study was begun in 1940. There is little doubt in the minds of most of these men that this "pale epithelium," regardless of its mode of origin, is apocrine tissue and should be so designated. Some of the more recent contributions to the literature from other institutions indicate that this thought is by no means provincially unique.

PRESENT STUDY

Material. Six specimens of axillary skin were removed without selection simply in order that the scent glands in human beings might be studied (Figs. 1 and 2).

Ninety-seven breasts were received in the surgical pathology laboratory directly from the operating rooms without any plan of selection except to accept whatever came in.

It had been noted previously by one of us (J. R. McD.) that there were tiny pinkish bits of tissue and equally tiny, bluish, frequently macroscopically cystic bits of tissue to be found in most breast specimens, and that these bits of tissue usually were composed of pale epithelium (Figs. 3, 4, 5, 6, and 7). Accordingly these were looked for and, if found, were removed in small blocks for sectioning and staining; if none were found, then blocks were cut at random from the breast. All specimen blocks were cut from the depths of the breast proper, the subcutaneous areas being avoided.

TABLE 1.—INCIDENCE OF PALE EPITHELIUM

Diagnosis	Breasts				
	Total	With pale epithelium			
		Number	Per cent	Macroscopic pink or bluish areas	
				Number	Per cent
Carcinoma	54	41	75.9	26	63.4
Chronic cystic mastitis	20	20	100.0	19	95.0
Chronic fibrous mastitis	7	3	42.8	1	33.3
Intraductal papilloma	7	6	85.7	5	83.3
Chronic mastitis	6	3	50.0	3	100.0
Chronic purulent mastitis	1	0			
Comedomastitis	1	0			
Fibrous atrophic mastitis	1	0			
Total	97	73	75.3	54	74.0

Pale epithelium was found in three-fourths of all the breasts examined, and in three-fourths of the instances in which it was present it could be found with the naked eye (Table I). It should be stated that the pink and bluish areas mentioned varied from 0.5 millimeter to 3 or 4 millimeters in diameter. Larger areas (always bluish) were not used, because the cystic dilatation and expansion had flattened the epithelium. The term "blue-domed cyst" has been applied by at least one man to these bluish structures, but since this term has been used in a grossly descriptive way—not implying any specific tissue but merely a gross, refractive phenomenon and a lack of malignancy—I feel that this term would be misleading if used to indicate these pale epithelial cysts (Table II).

Intracellular granules. The mere noting of intracellular granules in the pale epithelium was not difficult. The presence of granules of one kind or another was open to argument only in those instances in which the epitheli-

TABLE II.—INCIDENCE OF CYSTIC CHANGE IN PALE EPITHELIUM ON MICROSCOPIC EXAMINATION

Diagnosis	Breasts with pale epithelium		
	Total	Cystic changes	
		Number	Per cent
Carcinoma	41	33	80.4
Chronic cystic mastitis	20	20	100.0
Chronic fibrous mastitis	3	3	100.0
Intraductal papilloma	6	4	66.7
Chronic mastitis	3	3	100.0
Total	73	63	86.3

TABLE III.—INCIDENCE OF INTRACELLULAR GRANULES IN PALE EPITHELIUM AND OF POSITIVE STAIN FOR IRON

Diagnosis	Breasts with pale epithelium				
	Total	Intracellular granules		Positive reaction to stain for iron	
		Number	Per cent	Number	Per cent
Carcinoma	41	41	100.0	40	97.6
Chronic cystic mastitis	20	20	100.0	20	100.0
Chronic fibrous mastitis	3	3	100.0	3	100.0
Intraductal papilloma	6	5	83.3	5	83.3
Chronic mastitis	3	3	100.0	3	100.0
Total	73	72	98.6	71	97.3

um was moderately or considerably flattened as a result of cystic dilatation of the epithelial glands. As a rule, the granules were quite obvious. Sometimes they stood out in a most striking manner, showing extremely marked eosinophilia (Table III). There were several types of granules. The great majority were eosinophilic granules, large or very fine, which stood out even against the smoothly eosinophilic cytoplasm (Fig. 5). Then there were yellowish or brownish granules—present in only a few of the cells of any particular acinus of pale epithelium—which were even more readily visible in the sections stained with Berlin blue but which were apparently untouched by either of the two stains, Berlin blue or hematoxylin and eosin (Figs. 5 and 6).

Another type of granule was a very fine one—also not present in all the cells—which gave a fat reaction with the sudan III stain in the few such slides which were made. There were noted also some fat droplets, of varying size, in a few of the cells (Fig. 6).

Finally there was the type of granule which gave a positive reaction to the Berlin blue stain. Whether this one was identical with one of the previously mentioned types or represented a different metabolic stage of one of them was not established in this study. Certainly, when numerous markedly eosinophilic granules were seen in the section stained with hematoxylin and eosin, there was no correspondingly marked iron reaction in the section stained with Berlin blue. While there were usually a few cells found which contained a few or many granules giving a positive reaction to the stain for iron, there was not a universally present iron reaction in all the cells. There was extreme variation in the iron reaction, not only from cell to cell, but from gland to gland, or acinus to acinus, in the same slide. Although in a few instances there was a suspicion of a positive iron reaction in the cells of some of the regular mammary epithelium, this was not definite enough to deny the pale epithelium the uniqueness of this reaction.

Hyperplasia and papillary formation. Although papillary formation seemed to indicate growth activity, or even overactivity, it was sometimes noted when there was no evidence of hyperplasia. Usually, however, hyperplasia and papillary formation were seen together, and if hyperplasia were present, papillary formation was always present also (Table IV).

Hyperplasia was adjudged present principally on the basis of individual changes, differences and appearances of cells, and not merely because of an increase in the number of cells. If the nuclei of some of the pale epithelial cells were one and a half to two times as large as the nuclei usually seen and if they were hyperchromatic and contained multiple, large, hyperchromatic nucleoli or mitotic figures, then the cells containing them were considered hyperplastic (Fig. 8).

The myoepithelium. At first it was somewhat difficult to be certain about the myoepithelial cells (Fig. 6), but as more slides were examined and some very definite examples were seen, then the less obvious cells became more apparent. These cells are easily confused

with cells in the capillary walls lying immediately nearby, outside the basement membrane, but this confusion, noted in the literature, would seem more often to be due to cells, possibly reticular cells, which are seen actually in the basement membrane, which are very similar to the cells in capillary walls. The myoepithelial cells lie directly beneath the epithelium, above or on the basement membrane.

The myoepithelial cells are long, spindle-shaped, and not too numerous or closely packed in the unchanged gland or acinus. They seem, as a rule, to be thicker at the middle than do the usual reticular cells or the cells of the capillary walls and when they apparently participate in hyperplastic activity, they multiply into a definite layer and appear more like epithelial cells than the smooth muscle cells which they usually resemble.

Age. There was no great difference in average age between the group of patients whose breasts did contain pale epithelium and the group of patients whose breasts did not contain pale epithelium. The respective average ages were 47 and 49 years.

Relation of pale epithelium and papillary formation to the menopause. Sixty-five per cent of the specimens of breast with pale epithelium which showed papillary formation or papillary formation with hyperplasia, came from women past the menopause or in the midst of the menopause. This does not imply necessarily that the menopause, with its hormonal changes, is solely responsible for the occurrence of pale epithelium, but it might suggest that the menopausal and postmenopausal hormonal imbalances may be related to the histologic evidences of growth activity. Speert's experimental work with estrogenic hormones is very pertinent in these respects.

TABLE IV.—INCIDENCE OF PAPILLARY FORMATION AND HYPERPLASIA IN BREASTS WITH PALE EPITHELIUM

Diagnosis	Breasts with pale epithelium				
	Total	Papillary formation		Hyperplasia	
		Number	Per cent	Number	Per cent
Carcimona	41	20	48.8	13	31.7
Chronic cystic mastitis	20	9	45.0	8	40.0
Chronic fibrous mastitis	3	1	33.3	0	
Intraductal papilloma	6	2	33.3	2	33.3
Chronic mastitis	3	2	66.7	1	33.3
Total	73	34	46.6	24	32.9

COMMENT AND SUMMARY

There is little doubt in our minds that the pale epithelium discussed in this study, found in breasts and illustrated in Figures 3, 4, 5, 6, 7, and 8, is actually apocrine glandular tissue identical with the axillary apocrine scent glands (Figs. 1 and 2). This is not an original concept and this study has not conclusively proved the identity. Truly conclusive proof would rest on a cellular biochemical study, with identification of secretions from the tissue. Nevertheless, it would seem justifiable to consider this tissue to be apocrine scent gland tissue on the basis of similar staining and morphologic characteristics.

We have refrained, except where unavoidable for clarity's sake, from, referring to this pale epithelium as sweat glands, sweat gland epithelium, apocrine sweat glands or by any other term which is suggestive of sweat or sweat glands. Apocrine glands generally, the scent glands in particular, are not sweat glands, as Schiefferdecker showed. The latter term has been inappropriately and inaccurately applied to them, because they lie in the skin and morphologically are coiled glands. Their function in man has no bearing on the control of body temperature and they do not excrete large amounts of water and metabolites such as urea; instead, they elaborate a definite substance or secretion which itself has a role in the primitive animal economy.

The breast is an apocrine gland, on the basis of its mode of secretion; that is all that the term "apocrine" indicates. The breast is also a highly specialized modification of a certain primitive cutaneous gland, the latter being likewise parent to the scent gland (also an apocrine gland). Neither of these glands "sweats" in the manner of the epicrine or eccrine or true sweat gland. They secrete, rather than excrete, a definitely elaborated substance, the elaboration occurring in the cells of the glands. The excretory function of the eccrine gland,

on the other hand, is closely akin to that of the renal tubule.

The mere anatomic location of the scent glands, that is, in the skin, as well as some of their morphologic characteristics, led quite naturally to the inaccurate appellations "sweat glands," then "large sweat glands" and more recently "apocrine sweat glands." In the same way the breast is referred to as a modified sweat gland, though nobody considers that the breast "sweats" or that its secretion is sweat.

The term "apocrine glands," when applied to the breast, the scent glands, the ceruminous glands and so forth, is accurate as far as it goes, but it merely denotes a group of glands distinctive as to their method of secretion. Since these glands have also their origin, in common, the term "apocrine skin glands" might temporarily suffice as an over-all group name.

The scent glands could well be known, in addition and separately, as the scent glands, or odoriferous glands, or accessory sexual glands. Such terms have been suggested, as mentioned previously, and they are as fully individual and distinctive as the term "mammary gland," or the term "ceruminous gland." The pale epithelial structures encountered in the breast might then be referred to as "scent gland tissue in the breast," or "accessory sexual gland tissue in the breast." There is, of course, some redundancy here, since the breast might very well exhibit and contain such pale epithelium as an expected thing, inasmuch as the breast is a modification of the same primitive gland from which the scent gland is derived, and inasmuch as the scent gland, in its characteristics, does not seem to be far removed, or greatly modified, from the primitive glands. Hence, such epithelium might be considered the primitive epithelium, and its presence in the breast merely evidence of a reversion in part, even though the stimulus for such reversion might be a hormonal one.

Even more to be expected, perhaps, is the finding of this pale epithelium in supernumerary or accessory breasts, and especially in so-called aberrant breasts. As mentioned in the review of the literature, breastlike structures have been described on most parts of the body, including the extremities. There is no doubt about the finding of true breast tissue in the supernumerary or accessory breasts, but this does not necessarily indicate that all of the structures described as breasts or breastlike structures or aberrant breasts, actually are composed of breast tissue. Obviously, many of these structures are outside the embryologic milk-line and may well be, and probably are, hypertrophied apocrine glands of the more primitive, or scent gland, type. Even those which are *in* the milk-line and are more breastlike, may well be of the primitive type of apocrine gland but are simply further along in the differentiation to breasts as required of such glands lying in the milk-line. As H. E. Walter stated in 1903, no known mammal living or extinct has, or had, as many mammae as there are recorded sites for accessory breasts, so called. The only alternative explanation is that these "aberrant breasts" are really hypertrophied primitive apocrine glands, which, being outside the milk-line and therefore lacking the undefined embryologic and phylogenetic stimulus for specific organ formation, that is, breast formation, are unable to form true breasts. The gross caricature, therefore, is to be expected, and the misinterpretation thereby is easily explained.

As already mentioned, we consider the pale epithelium to be a relatively normal finding in the breast. If we consider the breast as a stable organ exhibiting little change except slowly and over long periods of time, then the occurrence of somewhat primitive epithelium, that is, the pale epithelium, could be considered definitely abnormal. However, as has been remarked by many workers (Ingleby and others), the breast is not "normal," it is not static, but it is a rapidly, frequently changing organ which is subject to many and diverse influences. Monthly it goes through a series of elaborate growth changes in preparation for a specific function. In view of these facts the finding of pale epithelium, that is, the presumptive primitive epithelium, not only does not seem extraordinary but seems to be "normal." This pale epithelium in the breast, however, might be explained somewhat differently. Its function may be to impart the characteristic mammalian, racial, and individual odor or odors to the milk, a hangover in the human being from more primitive evolutionary stages.

It is our impression that pale epithelium could be found in every breast, if diligently sought after. Although arriving at an entirely different conclusion about it, Dawson stated that the pale structures are to be expected in practically every pathologic and cystic condition of the breast, malignant or not. She found such structures in 116 of 120 breasts which were the sites of malignant lesions and in all of 48 cystic breasts. Prym, and Berka, however, reported pale epithelium in otherwise *normal* breasts, and it is our opinion that it can be found in any and all female breasts after the age of puberty. That it seems to be increased in quantity in breasts which are the sites of certain pathologic conditions, such as carcinoma and chronic cystic mastitis, seems to us further evidence of a hormonal relationship or dependency. The question of the possession of carcinogenic properties by hormones, especially the sexual hormones, is well known and is frequently discussed. If one assumes an excess or increased potency of certain ovarian hormones as a possible explanation, or cause, of chronic cystic mastitis and carcinoma of the breast, there is no reason to deny the assumption that side effects occur, such as an increase in the amount of pale epithelium in the breast. That pale epithelium will appear in response to the action of estrogenic hormones, for instance, would seem to be strongly suggested by Speert's experimental work. This may account for the easily noted high incidence of pale epithelium in breasts which are the sites of chronic cystic mastitis, for instance. This is not an original concept, other men having noted something of a relationship between chronic cystic mastitis and adnexal disease (48). The pituitary hormonal fractions undoubtedly play some direct or indirect role in this relationship and are under wide discussion in the literature.

Lee, Pack, and Scharnagel, have noted much more pale epithelium in the breasts of patients with oily skin and much body hair than in breasts of persons with less oily skin and less body hair. This again would indicate a pituitary-gonadal relationship which is necessarily hormonal in character. Semb found an increased incidence of chronic cystic mastitis in nulliparas, but made no study of the incidence of pale epithelium though, judging from the present study as well as others mentioned, the incidence should have been very high. The most obvious conclusion from all this would be that estrogenic hormone has direct control over the occurrence of pale epithelium in the breast, but the involved endocrine gland relationship in the human being would make this a risky conclusion without further experimental work.

In so far as chronic cystic mastitis is concerned, there is no doubt that the cystic changes occurring in the pale epithelium contribute to the grossly cystic character of the pathologic picture, and indeed some men consider the disease one solely of pale epithelial structures (4). In view of the frequent association of chronic cystic mastitis with carcinoma of the breast (30), it is even possible to explain on this basis the reported findings (our own also) of a relatively high incidence of pale epithelium in carcinomatous breasts.

The question that a malignant lesion, the so called sweat gland carcinoma of the breast, may arise from the pale epithelium is still debated. From a practical standpoint the tissue of origin of a carcinoma of the breast is of little significance to the patient, since low-grade carcinomas arising from the usual or "normal" mammary tissue have metastasized and killed, and since high-grade carcinomas similarly arising have apparently been cured. It would be of significance to determine the tissue of origin only if it were known, or could be shown, that carcinomas arising from pale epithelium were usually low grade, slow growing and slow to spread, or were usually high grade, fast growing, and fast spreading. This would then be of prognostic significance and value. However, as remarked by others (14), various gradations have been noted, as occurs among carcinomas arising from the usual or "normal" mammary tissue. This has been our experience. Of the 54 carcinomatous breasts which we examined, there were 8 malignant lesions (15 per cent) which *might* be termed so called sweat gland carcinoma, or more properly "scent" gland carcinoma of the breast (Fig. 9). However, the argument as to the distinction or separation of such carcinomas of the breast seems unnecessary and superfluous in

view of the close, intimate relationship, other than physical, of the tissues. On the other hand, the morphologic and staining distinctions of the pale epithelium in the breast would indicate a metabolic and functional distinction and difference, which in turn might result in, and indicate, quite different proliferative potentialities.

REFERENCES

1. Benda, C. Verh. deut. path. Ges., 1913, 16: 384.
2. Idem. Dermat. Zschr., 1894, 1: 94–110.
3. Berka, F. Beitr. path. Anat., 1912, 53: 284–323.
4. Berning, Heinrich, and Bücker, Joseph. Virchows Arch., 1937, 298: 728–742.
5. Brouha. Anat. Anz., 1905, 27: 311–317.
6. Cheatle, G. L., and Cutler, Max. Tumours of the Breast; Their Pathology, Symptoms, Diagnosis and Treatment. London: E. Arnold & Co., 1931.
7. Cheatle, Lenthal. Brit. J. Surg., 1935, 22: 710–715.
8. Cutler, Max. J. Am. M. Ass., 1932, 99: 2152–2156.
9. Dawson, E. K. Edinburgh M. J., 1932, 39: 409–438.
10. Deaver, J. B., and McFarland, Joseph. The Breast; Its Anomalies, Its Diseases, and Their Treatment. Philadelphia: P. Blakiston's Son & Co., 1917.
11. Dreyfuss, Robert. Virchows Arch., 1888, 113: 535–565.
12. Eggeling, H. von. Anat. Anz., 1904, 24: 595–605.
13. Ewing, J. Lectures on Tumor Pathology, lecture xxiv. Cornell Univ. Med. School, 1934.
14. Foote, F. W., and Stewart, F. W. Surgery, 1946, 19: 74–99.
15. Gates, Olive, Warren, Shields and Warvi, W. N. Am. J. Path., 1943, 19: 591–631.
16. Hamperl, H. Virchows Arch., 1939, 305: 171–215.
17. Herzenberg, Helene. Virchows Arch., 1927, 266: 422–455.
18. Horner, W. E. Special Anatomy and Histology. 8th ed., vol. 1, p. 342. Philadelphia: Blanchard & Lea, 1851.
19. Idem. Am. J. M. Sc., 1846, 11: 13–16.
20. Ingleby, Helen. Arch. Path., 1942, 33: 573–588.
21. von Kölliker, Albert. Manual of Human Microscopic Anatomy. (Translated by George Busk and Thomas Huxley; edited with notes and additions by J. Da Costa.) Philadelphia: Lippincott, Grambo & Co., 1854.
22. Kölliker. Quoted by Sheldon, W. H. (43).
23. Krompecher, E. Verh. deut. path. Ges., 1913, 16: 365–384.
24. Idem. Beitr. path. Anat., 1916, 62: 403–472.
25. Idem. Virchows Arch., 1924, 250: 495–516.
26. Kuzma, J. F. Am. J. Path., 1943, 19: 473–489.
27. Lee, B. J., Pack, G. T., and Scharnagel, I. Surg. Gyn. Obst., 1933, 56: 975–996.
28. Loeb, Leo. In Cowdry, E. V.: Special Cytology; the Form and Functions of the Cell in Health and Disease; a Textbook for Students of Biology and Medicine. Vol. 3, pp. 1631–1672. New York: Paul B. Hoeber, Inc., 1932.
29. Logie, J. W. Cancer Research, 1942, 2: 394–397.
30. MacCarty, W. C., and Mensing, E. H. Coll. Papers Mayo Clin. & Mayo Foundation, 1915, 7: 918–922.
31. Moullin, C. W. M. J. Anat. & Physiol., 1881, 15: 346–348.
32. Prym, P. Beitr. path. Anat., 1928–1929, 81:221–263.
33. Reclus, Paul. Bull. Soc. anat. Paris, 1883, 58: 428–433.
34. Idem. Rev. chir., Paris, 1883, 3: 761–775.
35. Rein, G. Arch. mikr. Anat. Entmech., 1881–1882, 20: 431–501.
36. Richter, Walter. Virchows Arch., 1932, 287: 277–296.
37. Robin, C. Am. J. M. Sc., 1846, 11: 439.
38. Salzmann. Quoted by Suzuki, Shigeru (45).
39. Schiefferdecker, P. Zoologica, 1922, 27: 1–154.
40. Schimmelbusch. Verh. deut. Ges., Chir., 1890, 19: 116–118.
41. Schimmelbusch, C. Arch. klin. Chir., 1892, 44: 117–134.
42. Semb, Carl. Acta chir. scand., 1928, 64 (suppl. 10): 1–484.
43. Sheldon, W. H. Arch. Path., 1941, 31: 326–337.
44. Speert, Harold. Surg. Gyn. Obst., 1942, 74: 1098–1105.
45. Suzuki, Shigeru. Jap. J. M. Sc. xiii, Dermat. & Urol., 1941, 2: 165–175.
46. Talke, Ludwig. Arch. mikr. Anat., 1903, 61: 537–555.
47. Idem. Beitr. klin. Chir., Tübingen, 1903, 38: 122–132.
48. Taylor, H. C., Jr. Surg. Clin. N. America, 1933, 13: 431–433.
49. von Walko. Quoted by Suzuki, Shigeru (45).
50. Walter, Alexander. Beitr. path. Anat., 1924–1925, 73: 142–167.
51. Walter, H. E. Anat. Anz., 1903, 22: 97–111.
52. Way, S. C., and Memmesheimer, Alois. Arch. Derm. Syph., Chic., 1938, 38: 373–382.
53. Weiner, H. A. Am. J. Cancer, 1937, 31: 373–403.

VAGINAL OPERATIONS FOR CYSTOCELE, PROLAPSE OF THE UTERUS, AND STRESS INCONTINENCE

WILFRED SHAW, M.A., M.D. (Cantab.), F.R.C.S. (Eng.), F.R.C.O.G., London, England

PERHAPS the most important factor in the etiology of prolapse is a loss of tone of the plain muscle tissue of the endopelvic fascia, and it is for this reason that the worst cases are seen in women of menopausal age or in postmenopausal patients. Other important factors are loss of tone of the levator ani muscles themselves and separation of the two levator muscles where they come together in the region of the perineal body as the result of lacerations during childbirth. The work of Halban and Tandler (2, 6) and Amreich (4), particularly, has emphasized the distinction between the endopelvic fascia and the pelvic fascia which covers the levator ani and obturator internus muscles. Although it may be difficult and sometimes impossible to define the endopelvic fascial layers by histology (Goff), they can be demonstrated quite easily at operation. Moreover, for successful plastic surgery in the treatment of prolapse, a detailed knowledge of the anatomy of the different layers is required. It is the purpose of this paper to call attention to certain anatomical details and to show how this knowledge can be applied to vaginal plastic surgery.

Vaginal Operations

ANATOMY OF THE VAGINAL WALLS

In the anterior vaginal wall immediately above the level of the urethral meatus and the anterior termination of the hymen, is a transverse groove which I have called the submeatal sulcus (Fig. 1, 5). I believe that the sulcus indicates the position of the urogenital diaphragm. In the anterior vaginal wall, about 3 centimeters above this level, is a second groove which I have called the transverse sulcus of the anterior vaginal wall. This sulcus corresponds approximately to the level of the junction of the urethra with the bladder, although it is produced as the result of the topography of an underlying fascial layer. The upper limit of the bladder in the anterior vaginal wall is defined by a sulcus which is best referred to as the bladder sulcus. A little above the level of the meatus in the anterior vaginal wall on each side is an oblique vaginal fold which passes downward and forward from the lateral side of the vagina. Between the transverse sulcus and the submeatal sulcus the vaginal wall is rugose.

In some cases of prolapse, the area of the vagina between the submeatal and transverse sulci is prolapsed and stretched, when the two sulci can be easily identified. At other times the two sulci remain approximately in their normal position. In cases of cystocele the main part of the prolapse is almost always between the transverse and bladder sulci. In the surgical treatment of cystocele the object should be to prevent the bladder from prolapsing in the area between the transverse vaginal and the bladder sulci.

ANATOMY OF THE VAGINAL FASCIAL LAYERS

If the cervix is pulled down in a case of prolapse so that the anterior vaginal wall is put on the stretch, and a midline incision made, a plane of cleavage, called by Amreich the vesicovaginal space, can be exposed. The vaginal layer of endopelvic fascia remains adherent to the vagina while the thin vesical fascia adheres to the bladder. The vaginal fascia varies in thickness whereas the vesical fascia is always thin and never well defined. The vesicovaginal space is relatively bloodless, and in operations for cystocele if the correct layer of cleavage is found, hemorrhage is reduced to a minimum. In old-standing cystoceles the space may be obliterated by fibrous tissue and separation is then only possible with a scalpel.

Between the transverse vaginal sulcus and the submeatal sulcus there is no plane of

From the Obstetrical and Gynaecological Department, St. Bartholomew's Hospital, London.

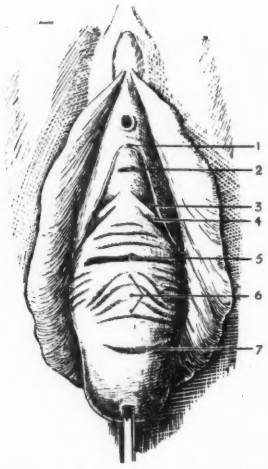


Fig. 1. Anatomical details of the anterior vaginal wall. *1*, The hymen. *2*, The submeatal sulcus. *3*, Paraurethral recess. *4*, Oblique vaginal fold. *5*, Transverse sulcus of the anterior vaginal wall. *6*, Arched rugae of the vaginal wall. *7*, Bladder sulcus.

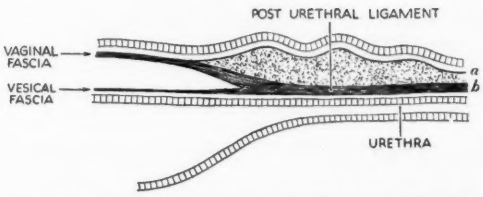


Fig. 2. Anatomy of the fascial layers in the vicinity of the external urinary meatus (diagrammatic). On the left the vaginal fascia and vesical fascia are separated by the vesicovaginal space. Nearer the urethra the vaginal fascia splits into two parts, a thin layer remains attached to the rugosed vaginal wall and is continued forward to point *a*. The greater part of the vaginal fascia fuses with the vesical fascia to form the posturethral ligament *b*. Between *a* and *b* the tissue is loose connective tissue, which must be cut through with the sharp end of a scalpel.

cleavage, for the vesical and vaginal fascias are fused in this area (Fig. 2). There is, however, a loose space in the vicinity of the rugosities, between the fused fascias and the skin of the vagina with its thin layer of vaginal fascia. A scalpel is required to separate the vaginal wall from the underlying fascial layers in this region.

The fascial tissues which lie deep to the vaginal wall between the submeatal and transverse sulci, form a specialized condensed layer of fascia which I have called the posturethral ligament. To appreciate the importance of the ligament, dissection should be made either on a cadaver or at operation in a case of cystocele of slight degree. The ligament extends from an attachment to the pubic ramus of one side, below and behind the urethra and the neck of the bladder, to the pubic ramus of the opposite side, and forms a dense sheet of tissue which supports the urethra and the neck of the bladder. The upper border is well defined and is responsible for the formation of the transverse vaginal sulcus. The ligament mainly consists of plain muscle tissue and if the muscle tone is lost the ligament stretches, which leads to urethrocele and contributes to the development of a cystocele. These views are different from those held by Kennedy. All gynecologists must have recognized the condensation of fascia around the urethra, and the term paraurethral fascia is sometimes used. In view of its condensed consistence, of the lateral attachments and the well defined upper border, in my view it should receive separate terminology, and I have suggested the term posturethral ligament.

Passing from the vesical fascia to the cervix and in consequence fixing the bladder to the cervix is a thin sheet of endopelvic fascia called the vesicocervical ligament (Amreich). On each side the ligament passes into the bladder septum which is a thicker layer of endopelvic fascia which attaches the bladder to the lateral aspect of the cervix. A plea for uniformity of terminology may conveniently be made at this stage. The various fascial layers are known to operating gynecologists, but gynecologists tend to use different names for the same structures. Such terms as subvaginal fascia, paravaginal fascia, pubovesical ligament, pubocervical ligament, pillars of the bladder, are employed. The terminology of Tandler and Amreich, which I have employed, seems to be the most exact and most scientific.

If the cervix is pulled down and the vesicocervical ligament stretched and then divided, a bloodless space is found between the bladder and the cervix. This space is called the vesicocervical space. The bladder cannot be mobilized unless this space is defined and until the bladder septa have been divided with scissors. Indeed, in my view the identification of the

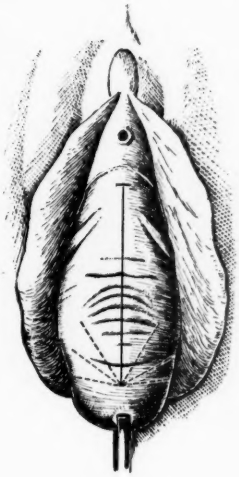


Fig. 3.

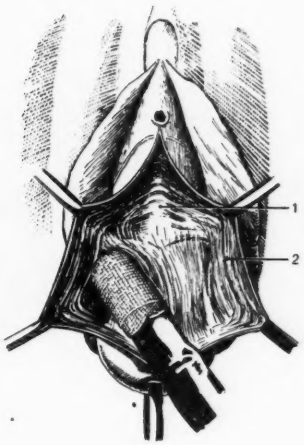


Fig. 4.

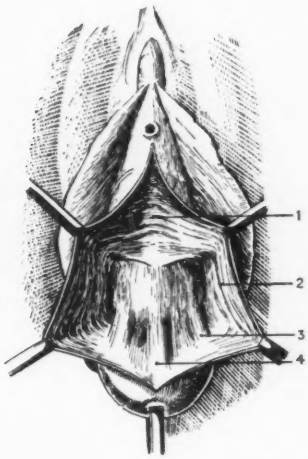


Fig. 5.

Fig. 3. Incisions employed for anterior colporrhaphy. The oblique lines indicate the inclination for different degrees of severity.

Fig. 4. Dissection in the vesicovaginal space. The bloodless layer is best found by stripping gently with gauze wrapped round the finger. *1*, Posturethral ligament *2*, Vaginal fascia.

Fig. 5. Exposure of the vesicovaginal space. *1*, Posturethral ligament. *2*, Vaginal fascia. *3*, Bladder septum. *4*, Vesicocervical ligament.

vesicocervical space is one of the most important steps in operations for prolapse.

OPERATIONS FOR CYSTOCELE

In cystocele the bladder prolapses in the area between the transverse vaginal sulcus and the bladder sulcus of the anterior vaginal wall. In some cases the posturethral ligament remains firm and hardly prolapses at all, while in other cases the ligament is stretched so that the transverse vaginal and the submeatal sulci are well defined on the prolapsed part. Theoretically, the objects of any cystocele operation are first, to mobilize the bladder and to return it to its normal position and secondly, to close the area between the upper border of the posturethral ligament and the cervix in such a way that the bladder will not prolapse again. It is insufficient to close the hiatus with the vaginal wall alone, for this may stretch again, nor is it satisfactory to close the space with the vaginal endopelvic fascia, the weakness of which is one of the fundamental causes of the development of the prolapse. This view is at variance with the present day practice. For many years I employed and devised different methods of pleating and overlapping the fascial tissues which intervene between the anterior vaginal wall and the bladder to form a supporting shelf. Experience has shown that such methods are unnecessary and the method which I describe in the following gives equally good results. The strongest supporting tissue in the vicinity is the posturethral ligament. For this reason I maintain that the bladder must be mobilized and pushed upward, and the space closed by suturing the posturethral ligament directly to the cervix itself. This is the fundamental principle of the operation.

I make a midline incision which ultimately passes from the submeatal sulcus to the bladder sulcus (Fig. 3). From the cervical end of this incision I make a lateral incision on each side. The inclination of the lateral incision depends upon the severity of the prolapse. First, the vesicovaginal space must be opened up. The space is found most easily at the cervical end of the incision. The best way is to apply traction to the lower angles of the vaginal flaps. I do not believe that there is any risk of injury to the bladder if ordinary care is

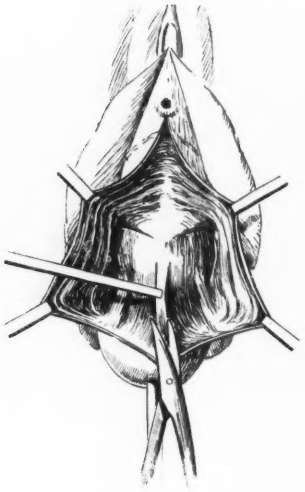


Fig. 6.

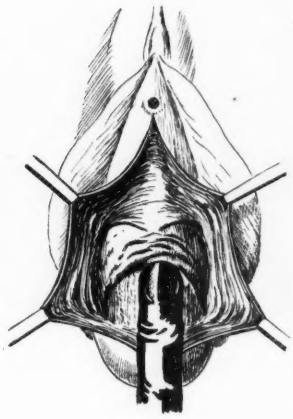


Fig. 7.

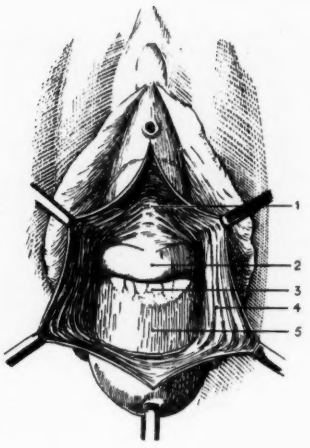


Fig. 8.

Fig. 6. Division of the vesicocervical ligament.
Fig. 7. After the vesicocervical space has been exposed the bladder is mobilized upward. The bladder septa must first be cut through.

Fig. 8. Exposure obtained after mobilization of the bladder. *1*, Posturethral ligament. *2*, Bladder. *3*, Peritoneum of the uterovesical pouch. *4*, Vaginal fascia. *5*, Front of the cervix.

taken. If the correct layer is found, the vagina, together with its fascia, strips easily and a few delicate touches with the scalpel, combined with separation with dry gauze wrapped round the finger, will open up the space as far upward as the posturethral ligament (Fig. 4). If the correct layer is found, there is little or no hemorrhage, for the vaginal vessels lie in the vaginal fascia and the vesical vessels lie in the vesical fascia. When the posturethral ligament is reached it is necessary to use a scalpel to cut through that part of the vaginal fascia which merges with the posturethral ligament, and over the surface of the posturethral ligament a scalpel must be used to separate the vagina with its rugose pouches from the ligament (Fig. 5). The next step is the usual division of the vesicocervical liagment, and the division must be carried sufficiently deeply to expose the bloodless white space of the vesicocervical space (Fig. 6). The bladder cannot be sufficiently mobilized, however, until the bladder septa have been divided to a moderate extent on each side. The bladder must be mobilized sufficiently so that it can be pushed upward to expose the uterovesical pouch of peritoneum (Fig. 7). The next step is to excise the redundant vaginal wall and its underlying fascia from the two lateral flaps, and it is at this stage that the vaginal vessels are divided and they must be ligatured separately (Figs. 8 and 9).

The crucial suture is now introduced. It passes through the vaginal wall and vaginal fascia, starting at a point 3 to 4 centimeters below the meatus, about ½ centimeter from the cut edge. The needle is passed through both the vaginal wall and the vaginal fascia (Fig. 10). It is then passed through the posturethral ligament on the same side of the midline. There is plenty of tissue to pick up, and there is no risk of injury either to the urethra or to the bladder. Before the suture is passed through the ligament the ligament should be pulled upward in the direction of the cervix and the ligament should be transfixed in the average case about half way between the submeatal sulcus and the cervical edge of the posturethral ligament. The suture is now passed through the front of the uterus. The level of the uterus at which the suture is introduced depends upon the severity of the case. The higher the level of the uterus at which it is introduced, the more the urethra will be

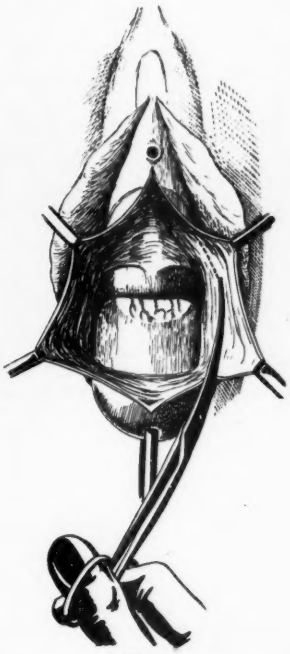


Fig. 9.

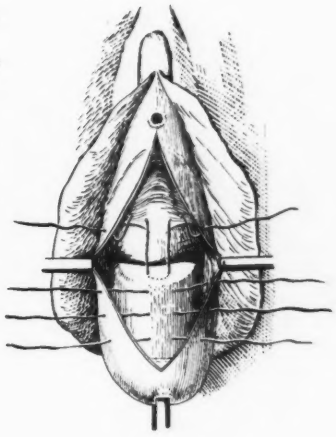


Fig. 10.

Fig. 9. Excision of the redundant vaginal wall together with the vaginal fascia.

Fig. 10. The key sutures. Above, the suture passes first through the vaginal wall together with its vaginal fascia, then through the posturethral ligament, then through the front of the cervix, then through the posturethral ligament and the vaginal wall of the opposite side. The lower sutures pass through the vaginal wall and the vaginal fascia, then through the front of the cervix and then through the vaginal fascia and the vaginal wall of the opposite side.

stretched, and sometimes it may be necessary to pass the suture through the uterovesical pouch. The suture is then passed through the posturethral ligament on the other side of the midline at a corresponding point and then through the vaginal fascia and vaginal wall as before. When this suture is tied the space through which the bladder can prolapse is obliterated completely (Fig. 11). Reinforcement sutures can be introduced when necessary.

In my view this particular suture is one of the most valuable in the whole of vaginal surgery for prolapse. Sometimes a series of interrupted sutures can be passed between the posturethral ligament and the front of the cervix, and many minor modifications of the technique are obviously possible. Clearly, one of the great advantages of the technique is that the urethra is stretched longitudinally, which is of the utmost service in the cure of stress incontinence.

No effort is made to dissect the vaginal fascia from the vagina and to interpose a layer of fascial tissues between the vaginal wall and the cervix, for the view is taken that the fascial layers are atonic in cases of prolapse and have little supporting action. The cervix part of the incision is now closed with interrupted sutures. Each suture passes through the vaginal wall and vaginal fascia, then through the front of the cervix and then through the vaginal fascia and vagina of the opposite side. This series of stitches should close still more the pre-existing space through which the bladder has prolapsed. At the other end of the incision it may be thought advisable to introduce a series of interrupted Lembert sutures through the posturethral ligament if there is a tendency to urethrocele or stress incontinence. The cut vaginal wall is then closed by a series of interrupted sutures.

A self-retained catheter is introduced into the bladder and retained for at least 5 days. It is found in practice that most patients have great difficulty in voiding urine for nearly a week after the operation. The end-results are extremely satisfactory.

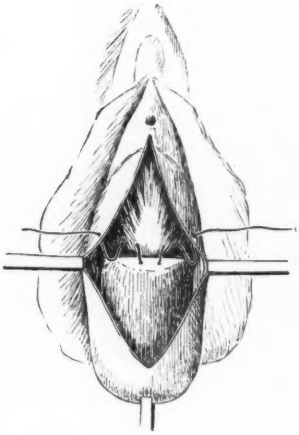


Fig. 11.

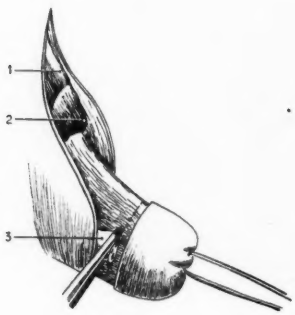


Fig. 12.

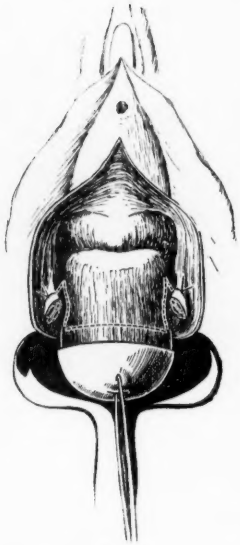


Fig. 13.

Fig. 11. The illustration shows how the tightening of the anterior key suture brings down the posturethral ligament and fastens it to the front of the uterus and cervix. In this way the ligament is elongated and the space through which the bladder has prolapsed becomes closed.

Fig. 12. Manchester-Fothergill operation. *1*, Posturethral ligament. *2*, The bladder. *3*, A clamp placed on the tissues which pass down laterally to the cervix.

Fig. 13. Manchester-Fothergill operation. After the lateral tissues have been ligatured the stump is mobilized by means of incisions placed immediately lateral to the cervix.

THE MANCHESTER-FOTHERGILL OPERATION

The principles of the method of anterior colporrhaphy are incorporated in the technique I use for the Manchester-Fothergill operation. A midline incision in the anterior vaginal wall is first made and the lateral incisions in the vicinity of the bladder sulcus are made at right angles, but are not at first carried round the cervix to circumcise the cervix. The lateral vaginal flaps are dissected away as before, the vesicocervical ligament divided and the bladder mobilized. The lateral vaginal flaps are excised and the key sutures passed through the vaginal wall, vaginal fascia, posturethral ligament and the front of the supravaginal portion of the cervix exactly as in the anterior colporrhaphy technique (Fig. 15).

The next step is to continue the lateral incisions around the cervix, and the level at which the incision is made depends upon how much of the cervix is to be removed. Next, on each side a strong curved clamp of the Weibel pattern is used to clamp the paracervical fascial tissues which enclose the vessels which run laterally along the cervix (Fig. 12). If prolapse of the uterus is well marked, the clamp is placed on the fascial tissues alone, but if the prolapse of the cervix is only of a moderate degree, it may be expedient to enclose the squamous epithelium layer covering the back of the cervix in the clamp, for the cut surface exposed after the cervix has been amputated can be covered with epithelium more easily if this step is taken.

The Manchester-Fothergill operation gives exceptionally good results in selected cases, probably because redundant vagina from the vicinity of the posterior fornix is stretched to cover the cut surface of the posterior half of the cervix. If there is well marked prolapse of the uterus, Mackenrodt's ligaments are stretched and the slackened ligaments must be tightened at operation. To carry out this procedure satisfactorily the following technique is employed. The cervix is amputated in the usual way and with the help of volsellum forceps the cut surface of the cervix is pulled to one side. With

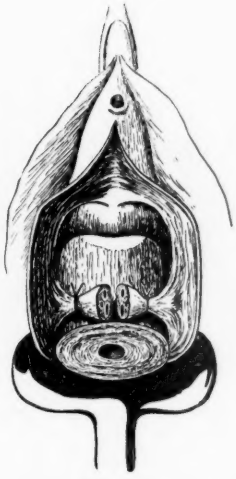


Fig. 14.

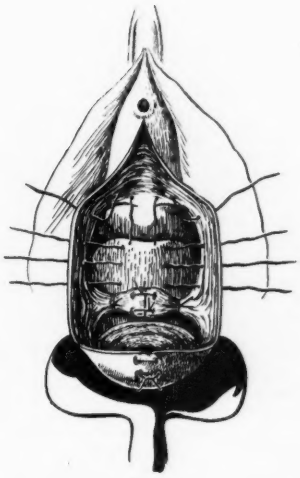


Fig. 15.

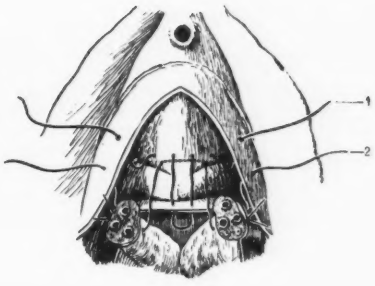


Fig. 16.

Fig. 14. Manchester-Fothergill operation. The cervix has been amputated and the lateral pedicles brought forward in front of the cervix.

Fig. 15. Manchester-Fothergill operation. The posturethral ligament is sutured to the front of the cervix as in the operation of anterior colporrhaphy, the lower sutures of anterior colporrhaphy are also introduced, while below the lateral pedicles are sutured together and also to the front of the cervix. The theoretical object is to define Mackenrodt's ligament and to put the ligaments on the stretch by stitching them to the front of the cervix in the midline.

Fig. 16. Vaginal hysterectomy for prolapse. Suture No. *1* passes through the vaginal wall and vaginal fascia, then through the posturethral ligament, then through the peritoneum. Afterward it passes through the corresponding structures of the opposite side. In this case the peritoneum replaces the uterus in the anterior colporrhaphy technique. Suture No. *2* passes through the vaginal wall and fascia, then through the stump containing the round ligament, ovarian ligament, and fallopian tube, then through the posturethral ligament, and afterward through the corresponding structures of the opposite side.

a scalpel the fascial tissues lying on the lateral side of the cervix are cut away from the cervix and mobilized for at least ½ inch above the level at which the Weibel clamp has been placed (Fig. 13). The same procedure is carried out on the opposite side. If the scalpel cut is sufficiently close to the cervix the risk of hemorrhage is small. Next, the tissues enclosed in the Weibel clamps are ligatured and the ligatures can then be regarded as being attached to the lower ends of Mackenrodt's ligaments. The next step is to suture these two ends to the front of the cervix in the midline and to pass a few interrupted sutures to stitch the two ends together (Figs. 14 and 15). The theoretical object of the technique is to define Mackenrodt's ligaments and to put the ligaments on the stretch by stitching them to the front of the cervix in the midline. Moreover, the technique tends to make the uterus anteverted. Some experience is required to determine the extent to which the fascial tissues should be mobilized. Obviously, if this method is to be employed, the Weibel clamp must not include any part of the vaginal epithelium. The cervix is then covered in the usual way by the Bonney-Sturmdorf technique.

VAGINAL HYSTERECTOMY FOR PROLAPSE

The variations possible in this technique are almost countless, for much depends upon the severity of the associated cystocele and prolapse of Douglas' pouch.

A midline incision in the anterior vaginal wall is first made, and the lateral incisions at the level of the bladder sulcus are placed transversely. The two vaginal flaps are dissected away as in the anterior colporrhaphy technique. The vesicocervical ligament is divided, the vesicocervical space is opened up and the bladder mobilized. If the cystocele is extensive, the bladder should be invaginated with a pursestring suture or with a series of

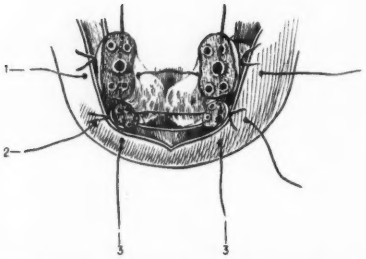


Fig. 17. Vaginal hysterectomy for prolapse. Suture No. *1* brings together the mid pedicle. Suture No. *2* brings together the pedicle of the uterosacral ligaments. If there has been an enterocele, suture No. *3* passes through the uterosacral ligament pedicle, then through the mid pedicle and passes in front to be sutured to the posturethral ligament. Sutures *1* and *2* of Figure 15 and suture *3* of Figure 16 are not tied until all three sutures have been introduced.

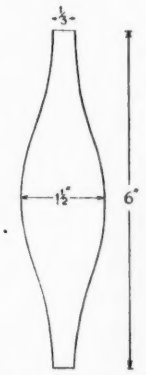


Fig. 18. The fascial strip taken from the fascia lata showing the approximate measurements.

reefing sutures. The uterovesical pouch is now opened up and the layer of peritoneum near the bladder grasped with long Kocher's forceps. The anterior wall of the uterus is pulled through this opening in the peritoneum, and the fundus of the uterus drawn downward. A series of Weibel's clamps is next placed along each side of the uterus and the uterus separated with a scalpel as far down as the uterosacral ligaments. The cervix is drawn upward and the circumcision of the cervix completed by joining the lateral ends of the original incision behind the cervix. The situation of this posterior incision through the vaginal wall depends upon the extent of the enterocele. The next step is to draw the fundus of the uterus downward and to put on the stretch the herniated peritoneum of Douglas' pouch. In this way the peritoneum can be mobilized and the hernial sac, if present, can be excised with scissors. After this, the uterosacral ligaments are clamped and the uterus removed by cutting with a scalpel on the uterine side of the clamps. I now place ligatures around the tissues enclosed in the clamps but do not remove the clamps themselves at this stage. A series of key sutures is then introduced (Fig. 16). The first passes through the vaginal wall and vaginal fascia about 1½ inches below the level of the urinary meatus. It then passes through the posturethral ligament half way between the meatus and the cervical edge of the posturethral ligament. Next, it passes through the peritoneum which was grasped in the Kocher's forceps, after which it passes through the posturethral ligament of the opposite side and then through the vaginal fascia and vaginal wall of this side. The suture is not tied at this stage. A second key suture is now introduced. It passes through the vaginal wall and vaginal fascia at a point a little below the introduction of the previous stitch. It then passes through the tissues enclosed in the first clamp which consist of the fallopian tube, round ligament and ovarian ligament. It passes through the posturethral ligament of the opposite side, then through the tissues enclosed in the corresponding Weibel's clamp of the opposite side, and out through the vaginal fascia and vaginal wall. The first suture is now tied and this brings together the vaginal fascial and the posturethral ligament, and draws down the peritoneum to stitch it to the posturethral ligament. In this way an excellent support is obtained which tends to prevent the bladder from herniating again. As a result of the second suture a shelf is formed by the tissues of the upper part of the broad ligament which also prevents the bladder from herniating again.

Next, if there has been a well marked enterocele the uterosacral ligaments are sutured directly to the posturethral ligament and subsequently with a series of interrupted sutures it is possible to suture the two uterosacral ligaments together, but this necessitates

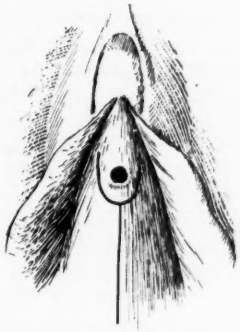


Fig. 19.

Fig. 19. Operation for stress incontinence. The incision is semicircular around the external meatus, with a prolongation upward in the midline along the anterior vaginal wall. The incision allows the lower part of the urethra to be mobilized.

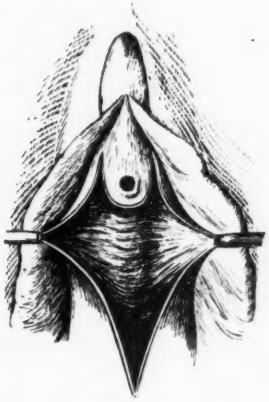


Fig. 20.

Fig. 20. In this step the lateral flaps are being dissected away in order to expose the urethra along its whole length.

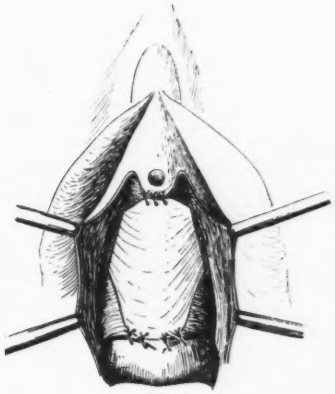


Fig. 21.

Fig. 21. The sling has been sutured in position. Above, one edge of the broad part of the sling has been sutured to the skin remaining around the urethral meatus. It is not advisable to introduce stitches into the wall of the urethra in this region. The other edge of the sling is sutured directly to the cranial margin of the posturethral ligament. On each side the thin ends of the sling pierce the tissues lying lateral to the urethra.

making a longitudinal incision in the posterior vaginal wall from the opening in Douglas' pouch otherwise the ligaments cannot be exposed sufficiently accurately (Fig. 17). The tissues contained in the other clamps are sutured together by the usual Mayo-Ward method, and it is often expedient to delay this suturing until this stage of the operation has been reached.

OPERATIONS FOR STRESS INCONTINENCE

Vaginal operations for the relief of stress incontinence have one factor in common—the originators always claim good results. It is doubtful whether the Stoeckel-Goebell technique, or the more modern Aldridge method of sling operation, should be employed unless efforts at vaginal repair have failed. I am quite satisfied that if the urethra is elongated in the methods I have described for anterior colporrhaphy, the Manchester-Fothergill operation, and vaginal hysterectomy, the stress incontinence is usually relieved provided that the elongation is of a sufficient degree. Furthermore, it is quite simple to interpose an additional supporting shelf beneath the urethra by a series of Lembert's sutures through the posturethral ligament. Indeed, I have obtained better results by such methods than by the Kelly technique. The etiology of stress incontinence is obscure and I am convinced that there are many underlying etiological factors. Some of the worst cases result from anterior colporrhaphy when, I believe, the nerve supply to the voluntary urethral sphincter is divided. In the average case of stress incontinence the external meatus is patulous and prolapsed downward and forward, and together with the lower ½ inch of the urethra projects well below the inferior pubic angle.

I think most gynecologists will agree that in a certain proportion of cases, stress incontinence recurs after relatively simple vaginal operations. Moreover, the worst cases to deal with are those in which the symptom is present without accompanying cystocele or prolapse of the uterus. Often, the only physical signs are a patulous external meatus combined with prolapse of the urethra and the lower third of the anterior vaginal wall. I have never been particularly impressed with the Stoeckel-Goebell or the Aldridge operation, mainly because the fascial strips which act as a sling are too narrow. I have, therefore, attempted to

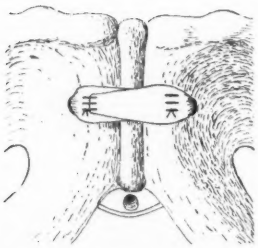


Fig. 22. The ends of the sling sutured together in front of the symphysis pubis (diagrammatic). The lower end of the sling can be seen supporting the urethra.

correct the condition by interposing a strip of fascia lata between the anterior vaginal wall and the urethra and supporting the two ends of the strip by boring two holes in the pubic bones and suturing together the ends of the fascial strip in front of the symphysis pubis. The fascia lata strip is fashioned so that it has a broad middle piece which can be sutured in place in such a way that it lies along the whole length of the urethra. Moreover, in some cases it may be convenient to suture the upper end of the strip to the front of the uterus itself. The operation details are as follows.

The strip must be 6 inches long and at least 1½ inches wide in its middle part, tapering to ends which need not be more than ⅓ inch in width (Fig. 18). An open operation is required and the severed edges of the fascia lata are sutured together with continuous catgut sutures combined with a few supporting mattress sutures. The fascial strip can be obtained and the wound closed in not more than 15 minutes.

The next step is to incise the vaginal wall in the midline by an incision which starts a few millimeters above the level of the external meatus and extends upward (Fig. 19). At the lower end, an incision is made around the urethra on each side in such a way that two lateral flaps can be dissected clear (Fig. 20). If there is an associated cystocele the incision must be carried upward to above the level of the bladder sulcus and the operation for anterior colporrhaphy performed in the usual way. If only a urethrocele is present it may not be possible to carry the incision so far upward. At this stage of the operation the object is to expose the urethra along the whole of its length, and the vaginal flaps must be dissected away laterally, the dissection being carried well out to the region of the pubic rami. The fascial strip is now taken and one edge of its midportion is sutured directly to the vaginal skin of a few millimeters thickness which remains around the meatus (Fig. 21). The opposite edge of the broad part of the fascial strip is sutured to the front of the cervix if the patient has been treated by the anterior colporrhaphy technique which I have already described. If, however, the bladder does not prolapse, the upper end of the broad part of the strip is sutured by a series of horizontal interrupted sutures to the upper limit of the posturethral ligament. In this way a broad sheet of fascia lata is placed in position to support the urethra.

The next step is to make a vertical incision on each side of the lower third of the urethra through the posturethral ligament and the underlying tissues until the retropubic space has been opened up.

The next part of the operation has as its object to bore a hole through each pubic bone about ½ inch from the midline of the symphysis pubis. Various methods have been employed to obtain a good exposure. It is possible to make an incision on each side along the groove immediately lateral to the labium majus ½ inch below the adductor longus tendon. This area is relatively bloodless. The labium majus is drawn inward and the pubic bone exposed by dissection and with the use of a rugine. The disadvantage of this method is that when the end of the fascia lata strip is drawn through the hole in the bone it must be sutured to the periosteum, for it cannot be sutured to the opposite end, so that the amount of tension on the sling is uncertain. Another method which I have employed has been to make an arched incision over the lower part of the symphysis pubis and the bodies of the pubic bones after first drawing the labia minora upward. The method gives a simple approach to the bones but it has certain grave disadvantages. In the first place, the urethra and the meatus tend to fall upward into the vagina when the patient is in the lithotomy position. Next, the holes made in the bones are too low down, so that the fascial sling is

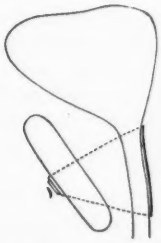


Fig. 23. Diagrammatic representation of the method of slinging up the urethra to the symphysis pubis. This illustration should be compared with the direction of the sling in the Aldridge operation. With the method illustrated there is no risk of kinking the urethra.

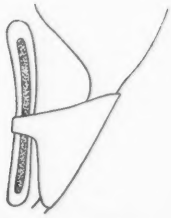


Fig. 24. The fascial sling is shown in position supporting the urethra, while to the left is the aperture through the pubic bone through which the end of the sling has been passed.

not supported in the correct direction. Another method is to make an arched incision with its upper limit at the level of the base of the clitoris which corresponds to about halfway down the symphysis pubis, with the lateral vertical limbs of the arch, each at about 1½ inches from the midline. It is a simple procedure to find the correct layer between the tendinous structures attached to the bones and the superficial tissues of the mons. Venous hemorrhage is troublesome just as in a Pfannenstiel incision, and great care must be taken to ligature every vessel because of the risk of the development of a hematoma. Experience has shown that the most satisfactory of the three methods of approach is by means of the incisions lateral to the labia majora. Excellent results have been obtained and it does not seem to be of importance to gauge the amount of tension placed on the sling with very great accuracy. It seems necessary only to suture the ends of the sling to the periosteum and the tendinous structures attached to the bones. The bodies of the pubic bones are cleaned with a rugine and the bones are perforated about ½ to ¾ inch from the midline with a simple brace and drill. An assistant can introduce a finger through the vagina into the retropubic space to prevent damage to the bladder. There seem to be no technical difficulties in drilling the bone and there seems to be little risk of damage to the bladder. One of the most difficult parts of the operation is to bring the ends of the fascial strip through the drill holes. A piece of catgut is tied to the end of the fascial strip and a long curved needle, 3 inches in diameter, is passed, eye end first, from in front, through the drill hole, then behind the pubic bone through the incision in the posturethral ligament, and the catgut attached to the strip threaded through the eye of this needle. The needle must be of the correct size and have a full half-circle curvature. The end of the strip can then be brought out through the front of the drill hole in front of the pubic bone. The two ends are then sutured together and the correct amount of tension obtained (Fig. 22). It is an extraordinary sight to see how the urethra can be pulled up to lie in the correct position. This part of the operation compares most favorably with the other methods of sling operation. With the other methods of approach a few sutures are introduced to attach the strip to the periosteum near the trephine hole. Penicillin powder is now introduced into the wound, particularly near the trephine holes. The great objection to drilling the pubic bones is the theoretical risk of osteomyelitis, although this complication did not develop in any of my cases. I felt therefore that the operation would be simplified if the end of the fascial strip were brought out through the lower angle of the obturator foramen. Much time was spent working with models and although I realize that the sling support is not so effective in direction when the ends are brought out through the obturator foramina, I tried out the method in a few cases and obtained excellent results. At the present time I have abandoned the method of drilling the pubic bones except for what I regard as severe cases. In the method of bringing the ends of the sling through the obturator foramen, vertical incisions are made on the

outer sides of the labia majora and the tissues are cut through down to the obturator foramen with a scalpel. A specially curved forceps with toothed ends is then passed through the obturator foramen in front and brought down lateral to the urethra as in the other methods, and the end of the strip is sutured to the deep tendinous tissues in the vicinity of the obturator foramen. The operation is extremely simple to perform and the results obtained are satisfactory.

Up to the time of writing, 25 patients have been operated upon, and the end-results have been extremely satisfactory. My own impression is that the results are already far better than those I have obtained with the Aldridge operation, and the broad support of the sling is obviously theoretically correct.

The characteristic optimism of all originators of operations for stress incontinence has been discounted so far as possible. Fundamentally, the idea behind the operation is to replace the posturethral ligament by the strip of fascia lata. Only time will show whether the fascia will produce a permanent support. The method has other possibilities, for a wide sling might be used in the treatment of severe degrees of cystocele.

Summary

1. The anatomical details of the grooves, rugosities, and folds of the anterior vaginal wall have been described.

2. The anatomical relations of the endopelvic fascia in the vicinity of the anterior vaginal wall have been discussed.

3. A condensation of the endopelvic fascia behind the urethra has been described and the term posturethral ligament has been used to describe this band.

4. An attempt has been made to describe the operation of cystocele on a purely anatomical basis, and a method of suturing the posturethral ligament to the cervix has been described.

5. Details have been given of the method of using the posturethral ligament in the operation of vaginal hysterectomy for prolapse, and in the Manchester-Fothergill operation.

6. A new method of sling operation for stress incontinence has been described. It consists of utilizing a sheet of fascia lata as a sling behind the urethra and bringing the two ends together through holes bored through the pubic bones.

References

1. Goff, B. H. Surg. Gyn. Obst., 1931, 52: 32.
2. Halban, J., and Tandler, J. Anatomie und Etiologie der Genitalprolapse bein Weibe. Vienna and Leipzig: Braumuller, 1907.
3. Kennedy, W. T. Am. J. Obst., 1937, 34: 576.
4. Peham, H. von, and Amreich, J. Operative Gynecology. Vol. 1. Philadelphia and London: J. B. Lippincott Co., 1934.
5. Shaw, Wilfred. Brit. M. J., 1947, 1: 477
6. Tandler, J. Veit's Handbuch der Gynaekologie. Edited by Dr. W. Stoeckel. Vol. 1, part 2, p. 342 Munich: J. F. Bergmann, 1926.

EXPERIMENTAL PULMONARY EMBOLISM

WILLIAM D. HOLDEN, M.D., F.A.C.S., Cleveland, Ohio, BYERS W. SHAW, M.D., Cleveland, Ohio, DONALD B. CAMERON, M.D., Cleveland, Ohio, PATRICK J. SHEA, Jr., M.D., Emory University, Georgia, and JOHN H. DAVIS, Jr., M.D., Cleveland, Ohio

THIS experimental study was conceived with the object of determining whether or not pulmonopulmonary, pulmonovagal depressor, and pulmonocoronary reflexes contributed to the death of animals subjected to massive pulmonary embolism. The literature is extensive on this subject and has been reviewed by Horn, Dack, and Friedberg in 1939 and Currens and Barnes in 1943. Reference will be made only to articles pertinent to the present study.

One of the principal objections to experimental studies on pulmonary embolism is that the embolus does not simulate that found in the human being. For anatomic and histologic observations of the pulmonary parenchyma, any foreign body that occludes pulmonary arteries may be used. Progressive thrombosis of the pulmonary arteries and retrograde thrombosis into the right ventricle following lodgment of emboli in the pulmonary arteries are not well understood and may be of considerable clinical importance. Thrombosis superimposed on an embolus cannot be satisfactorily studied in the experimental animal that has an artificial foreign body occluding a pulmonary artery. This objection has been minimized in the present study.

Another objection that has been raised is that the depth of anesthesia in experimental work of this nature precludes accurate observation of reflex changes. Care was taken to avoid deep anesthesia and in practically all the animals, gentle manipulation of blood vessels in the periphery produced slight pseudoaffective responses.

Forty adult, healthy, mongrel dogs weighing 7 to 15 kilograms were lightly anesthetized with sodium pentobarbital administered intravenously. An endotracheal tube was inserted in those animals which were to have the thoracic cavity opened. A mechanical positive pressure respirator was attached to the tube. Both external iliac veins were exposed retroperitoneally up to the internal iliac veins. The common femoral veins were exposed and all branches ligated with No. 000 silk. Soft rubber bulldog clamps were applied to the external iliac veins just distal to the internal iliac veins. Five hundred units (0.5 c.c.) of thrombin were injected into each iliofemoral vein through a No. 27 needle. Five puncture sites were used on each side. Each vein was gently massaged two or three times to insure adequate mixing of the thrombin and blood. Within a few minutes a firm thrombus could be palpated through the wall of the vein. In the open chest preparation, the left costal cartilages were cut and the thoracic cage spread apart until adequate exposure of the base of the heart was obtained. A metallic cannula was inserted into the left common carotid artery and connected to a calibrated mercury manometer which recorded partially dampened pressures on a kymograph. A brass cannula, 15 centimeters in length, was inserted into the right atrium through the left external jugular vein. A column of 0.25 per cent sodium citrate was connected to the cannula and to a recording device to determine venous pressure directly. An electrocardiograph recorded the conventional three leads in 11 animals. After basal records of the arterial and right atrial pressures were taken, the clamps were simultaneously or consecutively removed from the iliac veins.

Twenty-five animals were used in studying the dynamics of pulmonary embolism without nerve section or intravenous papaverine. Three were used to establish a satisfactory method of recording pressures. One died during insertion of the atrial cannula. Nine died

From the Laboratory of Surgical Research, Western Reserve University, Cleveland, Ohio.
Presented in the Forum on Fundamenta Surgical Problems before the Clinical Congress of the American College of Surgeons, Los Angeles, 18-22, 1948.

within 5 minutes after release of the emboli. Twelve were sacrificed after apparently having recovered from the embolism. Of these 12 dogs, 8 had emboli obstructing the main pulmonary arteries. Four had embolic obstruction of only one pulmonary artery. After release of the emboli, the following characteristic sequence of events occurred. Within 2 to 5 seconds, the dog developed marked respiratory distress, a precipitous drop in arterial pressure, tachycardia, and an elevation in atrial pressure. In the dogs that succumbed, the respiratory rate increased, became irregular, and then slowed progressively during the ensuing few minutes. The depth of the respiratory excursion increased until only infrequent gasps were observed. During the same period, the arterial pressure dropped progressively, the cardiac rate became slower, and venous pressure rose several centimeters of water. In none of the 40 dogs was ventricular fibrillation or abrupt cessation of cardiac activity observed. Cardiac contractions became progressively slower and more feeble until all muscular activity ceased. Respirations invariably stopped in the closed chest preparations before cardiac contractions ceased. The initial stimulation of respiratory rate and depth can best be explained by the superior vena caval reflex described by Megibow, Katz, and Feinstein. The cessation of respiration, however, before cardiac activity ceased, accompanied in all instances a progressive systemic hypotension and was probably a dependent upon cerebral ischemia. In the open chest preparations, dilatation of the pulmonary conus, right ventricle, and atrium (Fig. 1) was striking in the dogs that did not survive. Distension of the coronary veins was noted.

The heart and lungs were examined immediately after death or sacrifice and sections taken whenever it was thought advisable. The right heart of all animals was dilated. The dilation, however, was less striking than in the living animal. The emboli were easily recognized and found consistently in the major pulmonary arteries (Fig. 1). On occasion embolic fragments were found caught in the chordae tendinae in the right ventricle and on 2 occasions embolic obstruction occurred at the tricuspid valve. The emboli were firm, homogeneous, and purplish-red. On many occasions, recently formed thrombi were observed extending into branches of the pulmonary arteries. They were also found in the right ventricle. They differed from the emboli in that they were soft and bright red. The last 13 animals were heparinized with 10 milligrams of heparin given intravenously after the thrombi were formed in the iliac veins. It was our impression that the heparinized animals underwent less severe changes in pressure after embolism. Individual variation, however, was sufficiently great so that no exact statement can be made on this aspect of the experiment. Examination of the pulmonary arteries of the heparinized animals revealed the emboli to be farther out in the divisions of the main pulmonary artery than was seen in the nonheparinized animals. The formation of thrombi in the branches of the pulmonary arteries was conspicuously absent in these animals. The left atrium and ventricle, aorta and inferior vena cava were routinely opened and on no occasion was the blood coagulated. Contrary to the findings of Megibow, Katz, and Feinstein, the lungs of the dogs that died within 2 to 10 minutes showed areas of atelectasis, and diffuse or focal ecchymosis. Figure 2 shows the two lungs of a dog that died 5 minutes after release of the emboli. Sections of the right and left lung are shown in Figures 3 and 4. Atelectasis, diapedesis of erythrocytes, and interalveolar hemorrhage are noted in Figure 4, whereas little change is observed in the lung that had only partial embolic obstruction of its artery (Fig. 3).

In the animals that survived the initial emboli, characteristic changes occurred in their cardiovascular dynamics. Arterial pressure dropped immediately 20 to 40 millimeters of mercury and returned to the initial level or above within 5 seconds to 1 minute. Right atrial pressure rose 20 to 40 millimeters of water and gradually over a period of 2 to 3 minutes returned to normal (Fig. 5). Respiratory changes were variable in this group. In general, the rate increased for a few seconds. The depth of respiration, however, increased or decreased and on occasion no change was noted.

In all but 1 of the experiments in which the animals survived the initial emboli, the pres-

Fig. 1. The pulmonary conus, right and left pulmonary arteries have been opened. Emboli lying in both pulmonary arteries can be seen. The right side of the heart is dilated and the distended coronary veins are seen.

sure in the right atrium promptly returned to normal levels. In view of this observation, it is unlikely that reflex vasoconstriction of the pulmonary arterial tree occurs in sublethal embolism. The readjustment of blood volume in the pulmonary circuit and the response of the right ventricle to the increased pulmonary resistance explain more simply the rise and fall of right atrial pressure.

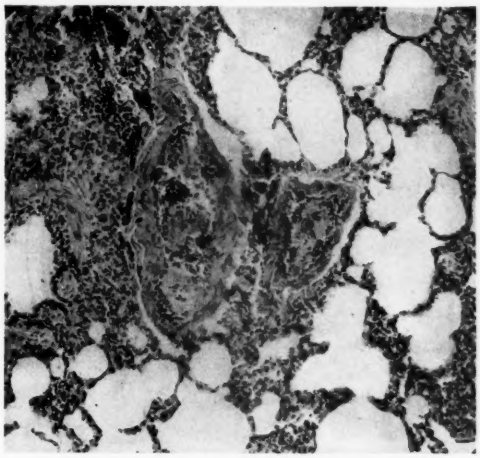


Fig. 3. The microscopic appearance of the relatively normal lung in Figure 2.

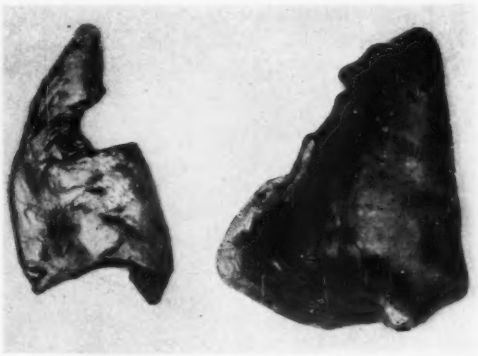


Fig. 2. Gross appearance of the right and left lung 5 minutes after a fatal embolus. The pulmonary artery to the lung on the left was partly obstructed. The glistening surface may be seen. Complete obstruction was present on the right and the ecchymosis and loss of luster are noted.

One of the most impressive observations made on these 40 animals was the marked degree of obstruction in the pulmonary arteries necessary to produce death. In many of the dogs that were sacrificed, a large part of the pulmonary circuit was obstructed and yet dynamic changes during the embolism had been slight and temporary. In these animals, however, there was reason to believe that with

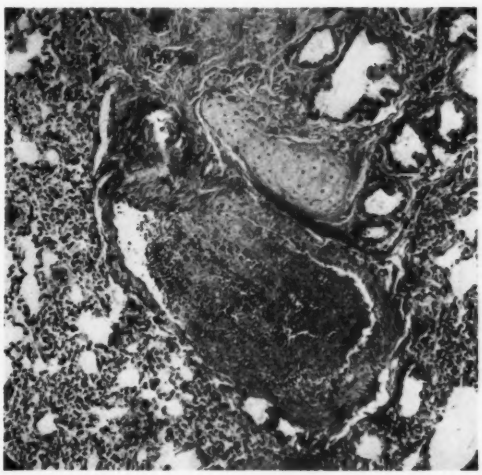


Fig. 4. The microscopic appearance of the lung whose pulmonary artery was completely obstructed (Fig. 2). Atelectasis and interalveolar hemorrhage are noted. A branch of the pulmonary artery containing an embolus can also be seen.

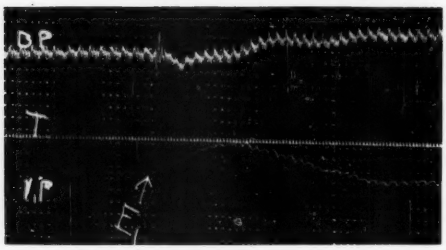


Fig. 5. The top record indicates left carotid blood pressure; the center is time in seconds; and the lower, right atrial pressure. *E* designates the release of the thrombi from the iliac veins. The fall in carotid pressure and the rise in atrial pressure were found in all animals.

superimposed thrombosis, death would have ultimately intervened.

Electrocardiographic tracings in 11 experiments showed no consistent alteration in pattern. Depression of the S-T segment in lead III was encountered in 6 dogs. Inverted and diphasic T waves were seen in lead III on 5 occasions. Prominent Q waves were observed 3 times in leads I and III. A shifting pacemaker was observed once and arteriovenous dissociation once. In fatal instances, gradual slowing of the auricular rate was seen. No ventricular fibrillation was recorded.

For many years, a controversy has existed concerning the presence or absence of pulmonovagal reflexes in pulmonary embolism. Schwiegk, Schweitzer, and Parin observed that distension of the pulmonary arteries produced a reduction of systemic arterial pressure that was abolished by section of the cervical vagi. Parin suggested that the systemic hypotension, not uncommonly observed in pulmonary embolism, may be due to such reflex activity. A pulmonovagal-coronary reflex reducing coronary blood flow has never been demonstrated experimentally but has been invoked on many occasions to explain death in pulmonary embolism. The suggestion that a pulmonocoronary reflex exists in pulmonary embolism is based in part on clinical evidence. Leriche, Fontaine, and Friedmann reported 30 per cent of their patients who died after pulmonary embolism had only partial occlusion of the pulmonary arteries. De Takats, Beck, and Fenn noted that a typical death from pulmonary embolism occurred in the presence of minor pulmonary obstruction in 7 out of 35 cases. On the other hand, Pilcher in a postmortem study of 40 patients who died following pulmonary embolism observed mechanical obstruction sufficient to cause death in 37. Karsner has never observed death as a result of a minor embolism without some contributing cause being present such as cardiac failure or coronary arteriosclerosis. Horn, Dack, and Friedberg observed that morphologic evidence of coronary insufficiency in cases of embolism of the pulmonary artery is more likely to occur if there are recurrent embolization, narrowing of the coronary arteries, cardiac hypertrophy, and adequate duration of life after embolism.

The experimental evidence in favor of a pulmonocoronary reflex has resulted from survival studies after cervical vagotomy and atropinization. Electrocardiographic studies before and after vagotomy and atropinization in pulmonary embolism have also contributed to the acceptance of such a reflex. Mosler, Radnai and Mosonyi, and Scherf and Schonbrunner, after studying electrocardiographic changes in pulmonary embolism and the results of vagal section and atropinization concluded that vagal stimulation had decreased coronary blood flow. Love, Brugler, and Winslow felt that similar electrocardiographic changes could be ascribed to mechanical obstruction of the pulmonary circuit. Malinow, Katz, and Kondo stated that bilateral cervical vagotomy did not abolish the electrocardiographic alteration produced by emboli in dogs and that there was no evidence for assuming the existence of a pulmonocoronary constricting reflex in pulmonary embolism. De Takats, Beck, and Fenn observed a 32 per cent mortality with atropine and 60 per cent with vagotomy in dogs which were subjected to embolism. A control series had a 100 per cent mortality rate.

Experimental work has demonstrated that mechanical obstruction of the pulmonary circuit is necessary to produce death. Mann introduced paraffin and blood clots formed in vitro into the venous circulation and found that death occurred only in the presence of considerable obstruction to pulmonary blood flow. Hall and Ettinger concluded that re-

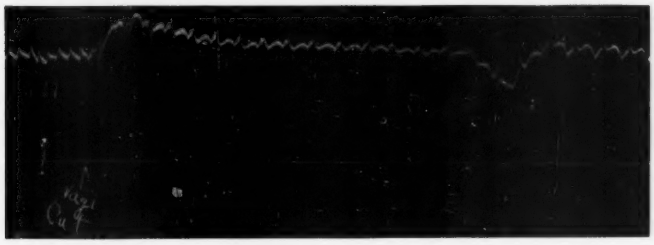


Fig. 6. The upper pressure recording is the carotid blood pressure and the lower, the right atrial. Cervical vagotomies were performed as indicated on the graph. The emboli were released at E_1. The same changes in pressures were observed. Tachypnea did not develop.

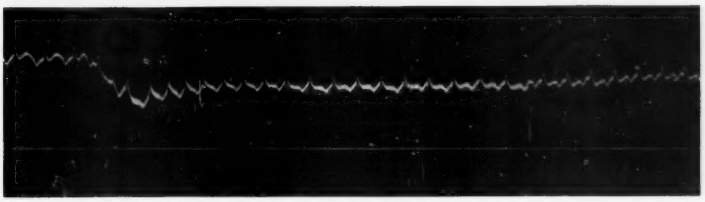


Fig. 7. This is a continuation of the record in Figure 6. At E_2 emboli were released. Seventy-five per cent of the pulmonary arterial circuit was occluded at autopsy.

flexes did not contribute to death in experimental embolism. Mendlowitz using a Penrose tube filled with dilute barium sulfate studied cardiac dynamics after a major embolism in dogs and concluded that the type of circulatory failure resulting was due only to mechanical obstruction of blood flow in the pulmonary circuit.

Eight dogs were subjected to cervical vagotomies and 4 dogs had resections of the stellate and upper four thoracic ganglia as well as vagotomies. Changes in hemodynamics were consistent and precisely what were encountered in the control experiments. Arterial pressures were reduced as rapidly and extensively as before. In the dogs that survived the initial emboli, arterial pressures returned to normal within 1 to 2 minutes. Changes and readjustments in right atrial pressure similar to those in the control animals were observed in this group. No more emboli were required to produce death than in the control series.

Protocol 32. A 15 kilogram dog was anesthetized with intravenous nembutal and an endotracheal tube inserted to insure a free respiratory passageway. The thoracic cavity was closed throughout the experiment. Left carotid and right atrial pressures were recorded as previously described. The pulse and respiratory rate were recorded. A three lead electrocardiogram was taken before and during the experiment. The external iliac veins were exposed retroperitoneally up to the common iliac veins. All branches of the external iliac and common femoral veins were ligated. Five hundred units of thrombin were injected into each common femoral and external iliac vein at 5 sites through a No. 27 gauge needle. The cervical vagi were exposed and sectioned. Figure 6 shows the result of the vagotomy and the pressure changes observed after release of the first emboli. Arterial pressure dropped 40 millimeters of mercury. A slight temporary reduction in pulse pressure was observed. Venous pressure rose 25 millimeters of water and the depth of respiratory excursions increased. The dog recovered within 2 minutes. Ten minutes later a second embolus was released. The same change in dynamics occurred except several minutes transpired before recovery was complete (Fig. 7). A third embolus was released with similar alterations in pressures observed, following which the animal was sacrificed by injecting 10 cubic centimeters of nembutal intravenously. The thoracic viscera were examined. Multiple areas of ecchymosis and atelectasis were observed in all lobes of the lungs. The right heart was dilated and coronary veins distended. On opening the heart, the left ventricle and atrium contained a small amount of bright red blood. The right pulmonary artery was obstructed by a large embolus. The left pulmonary

Fig. 8. Both vagi and upper thoracic sympathetic chains were removed. The emboli were released at E_1. The upper record shows the profound drop in carotid pressure. The lower record is right atrial pressure.

artery contained an embolus which occluded no more than 50 per cent of its lumen. An embolus was lodged between chordae tendinae in the right ventricle.

Protocol 39. This animal was prepared as all others. In addition, however, the cervical vagi, stellate ganglia, and thoracic sympathetic chains (T_2 to T_5) were removed. The thoracic cavity was then closed while positive pressure was applied to the respiratory tract through an endotracheal tube. Figure 8 shows the immediate reduction in arterial pressure and rise in venous pressure with death ensuing 2 minutes after release of the embolus. Obstruction of both pulmonary arteries was found at autopsy.

Dog 38 was subjected to both bilateral vagotomies and cervicothoracic sympathectomies. After release of the emboli, arterial pressure fell and venous pressure rose transiently in the same manner as was observed in the control animals.

Papaverine has been enthusiastically advocated in the treatment of pulmonary embolism. The use of this drug is based on the well known clinical and experimental observation that embolic obstruction of a peripheral artery induces in many instances an intense spasm of the arterial tree of the extremity, both distal and occasionally proximal to the site of obstruction. It is also well established that papaverine relaxes smooth muscle (Pal), and produces vasodilatation (Macht, 16, and Macht, Herman, and Levy, 17). From these facts, it has been postulated that a pulmonopulmonary vasoconstricting reflex occurs in pulmonary embolism and that it may be advantageously abolished by the administration of papaverine. Collins, de Takats, Denk, Burk, Domanig, Katz, and Barnes have advised the use of papaverine to relax the pulmonary arterial system. Jesser and de Takats in an experimental study showed that the vascularity of the pulmonary arterial tree increased after the intravenous administration of papaverine immediately following embolism of a major artery. No conclusions could be drawn, however, as to the presence of arteriospasm before the use of papaverine or arteriodilatation afterward. In a series of 10 dogs subjected to massive embolism and given papaverine, they obtained a mortality rate of 40 per cent, whereas a control group of 25 all succumbed. Bradshaw and Chodoff studied the effect of eupaverine on the pulmonary circulation of 29 cats. Transient depression of the systemic pressure and transient elevation of the pulmonary pressure were consistently found. After embolization with oil, similar but greater changes occurred.

Three dogs were given papaverine intravenously before and after embolization in doses ranging from 0.0032 to 0.016 gram. Similar changes were observed in the 3 experiments. Dog 34 was given 0.0032 gram of papaverine intravenously. The systemic arterial pressure fell abruptly but returned to normal levels within 20 seconds. The decrease in atrial pressure was observed on several other occasions and is not in accord with Bradshaw and Chodoff's observations. The most striking feature of all papaverine injections, however, was the transient nature of the effects on the cardiovascular system. Figure 9 shows the result of administering 0.0032 gram of papaverine im-

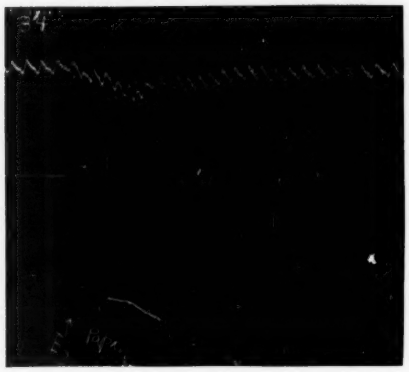


Fig. 9. An embolus was released at E_2. The reduction in carotid pressure (upper) and elevation of right atrial pressure (lower) are seen; 0.0032 gram of papaverine was administered intravenously and a secondary drop of carotid pressure is noted. The temporary interruption of the rising right atrial pressure is seen also.

mediately after release of emboli. A temporary reduction of atrial pressure occurred but it was immediately followed by a persistent elevation. This same dog was subsequently given 0.016 gram of papaverine intravenously with the characteristic depression of both carotid and right atrial pressures (Fig. 10). At autopsy it was estimated that 90 per cent of the pulmonary arterial circuit was obstructed with emboli in the main pulmonary arteries. Atelectasis and ecchymotic areas were observed in all lobes except the right lower.

Dog 35 was given 0.0064 gram of papaverine intravenously and displayed a reduction in systemic pressure of 40 millimeters of mercury but no change in atrial pressure. Thirty seconds later, emboli were released and the customary changes in pressures were observed. After stabilization of the pressures had occurred, the experiment was repeated with the same results. Papaverine given 2 minutes after recovery produced depressions of carotid pressure and right atrial pressure which returned to normal in 30 seconds. After pressures had become stabilized, embolization was repeated followed by papaverine in 2 minutes. Again reductions in arterial and atrial pressures were observed. At autopsy, a saddle embolus was found with moderate patchy atelectasis and intrapulmonary hemorrhage.

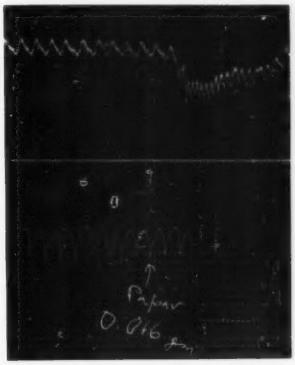


Fig. 10. This record is a continuation of Figure 9; 0.016 gram of papaverine administered intravenously temporarily depressed both carotid and right atrial pressures.

DISCUSSION

It cannot be denied that deleterious reflexes may contribute to death in pulmonary embolism in the human being. It would, indeed, be strange if autonomic reflex activity did not increase when a large portion of the pulmonary circuit is suddenly obstructed.

Our experimental findings do not support such a view but are more in accord with the conclusions of Hall and Ettinger and Mendlowitz. In the 40 dogs studied in this series, no hemodynamic changes were observed that could not best be explained on a mechanical basis. Depending upon the amount of pulmonary obstruction, systemic arterial pressure fell moderately or slightly and recovered promptly as blood flow through the unobstructed portion of the pulmonary circuit increased. As obstruction became more complete, systemic pressure fell progressively until death occurred. Pressure in the right atrium rose in a fashion corresponding to the depression in arterial pressure. No dogs died suddenly suggesting coronary artery spasm. All the dogs who were subjected to vagal section and removal of the stellate and upper thoracic sympathetic ganglia exhibited the same dynamic changes as the control group.

Our experience is in accord with Katz's suggestion that electrocardiographic patterns suggesting coronary insufficiency are the result of a combination of reduced aortic pressure and increased pressure in the right heart interfering with venous drainage from the myocardium.

So far as a pulmonopulmonary reflex is concerned, there is no evidence in this study that such exists. In all instances of embolism, whether the vagi and sympathetic chains are intact or not, the changes in systemic and right heart pressures are transient if the dogs survive and are readily explained on a basis of mechanical readjustment of pulmonary circulation. In the animals that succumb, systemic pressure becomes progressively lower and right atrial pressure higher. These animals all have at least 70 per cent of the pulmonary circuit mechanically obstructed. On no occasion was a persistent elevation of right atrial pressure observed which could be explained on a basis of pulmonary arterial spasm.

The reduction of right atrial pressure after the administration of papaverine could be in-

terpreted as being the result of relaxation of the pulmonary arterial tree. It could be associated as well with relaxation of the venae cavae entering the heart. The simultaneous depression of atrial and arterial pressures after giving papaverine and their concomitant recovery are more indicative of a generalized arterial and venous dilatation than relief of a localized pulmonary arteriospasm. If the temporary reduction in atrial pressure were due to pulmonary arterial dilatation, an increased filling of the left heart and rise of systemic pressure could be anticipated. This was not seen.

A patient was recently observed by one of us who was apparently recovering from the initial hypotension produced by a large pulmonary embolus. Immediately after the intravenous administration of 0.032 gram of papaverine, the blood pressure dropped, pulse rate, dyspnea, and cyanosis increased for a period of 2 to 3 minutes. The patient recovered and no opportunity for determining the occurrence of a second embolus was possible. It was considered likely that the dramatic clinical changes resulted from the administration of the papaverine.

In view of the consistent reduction in arterial pressure observed in all experimental studies after papaverine has been administered, any benefits derived from the use of this drug in major pulmonary embolism appear doubtful. All of the animals that died in these experiments did so in a state of marked hypotension. Respirations ceased in all instances before cardiac activity was arrested. To embarrass further the circulation to medullary centers by depressing systemic blood pressure does not seem warranted. If the administrations of papaverine were of value, its transient effect would exclude any therapeutic benefit.

CONCLUSIONS

1. Pulmonary embolism closely simulating that occurring in human beings was produced experimentally.

2. No evidence was obtained from these experiments to support the supposition that pulmonopulmonary, pulmonocoronary, or pulmonovagal depressor reflexes contribute to the death of dogs after massive pulmonary embolism.

3. It is suggested as a result of this work that the use of papaverine in the treatment of massive pulmonary embolism is without benefit and may indeed be harmful.

4. The constant absence of postembolic thrombosis in the pulmonary arteries of the heparinized animals suggests that the early intravenous administration of heparin to patients may be of great value.

REFERENCES

1. Barnes, A. R. J. Am. M. Ass., 1937, 109: 1347–1353.
2. Bradshaw, H. H., and Chodoff, R. J. Surg. Gyn. Obst., 1940, 70: 768–772.
3. Burk, W. Zbl. Chir., 1938, 65: 140–142.
4. Collins, D. C. Am. J. Surg., 1936, 33: 210–219.
5. Currens, J., and Barnes, A. R. Arch. Int. M., 1943, 71: 325–344.
6. Denk, W. München. med. Wschr., 1934, 81: 437–439.
7. De Takats, G., Beck, W. C., and Fenn, G. K. Surgery, 1939, 6: 339–367.
8. Domanig, E. Zbl. Chir., 1937, 64: 1161–1162.
9. Hall, G. E., and Ettinger, G. H. Canad. M. Ass. J., 1933, 28: 357–368.
10. Horn, H., Dack, S., and Friedberg, C. K. Arch. Int. M., 1939, 64: 296–321.
11. Jesser, J. H., and de Takats, G. Arch. Surg., 1941, 42: 1034–1041.
12. Karsner, H. T. Personal communication.
13. Katz, L. N. Dis. Chest, 1945, 11: 249–255.
14. Leriche, R., Fontaine, R., and Friedmann, L. J. chir., Par., 1937, 50: 737–748.
15. Love, W. S. Jr., Brugler, G. W., and Winslow, N. Ann. Int. M., 1938, 11: 2109–2123.
16. Macht, D. Arch. Int. M., 1916, 17: 786.
17. Macht, D. I., Herman, N. B., and Levy, C. S. J. Pharm. Exp. Ther., 1916, 8: 1–37.
18. Malinow, M.R., Katz, L. N., and Kondo, B. Am. Heart J., 1946, 31: 702–710.
19. Mann, F. C. J. Exp. M., 1917, 26: 387.
20. Megibow, R. S., Katz, L. N., and Feinstein, M. Arch. Int. M., 1943, 71: 536–546.
21. Mendlowitz, M. J. Thorac. Surg., 1938, 8: 204–218.
22. Mosler, E. Med. Klin., Berl., 1931, 27: 1555–1557.
23. Pal, J. Wien. med. Wschr., 1913, 63: 1049–1052.
24. Parin, V. V. Am. J. M. Sc., 1947, 214: 167–175.
25. Pilcher, R. Lancet, Lond., 1939, 1: 1257–1258.
26. Radnai, P., and Mosonyi, L. Zschr. ges. exp. Med., 1936, 98: 651-661.
27. Scherf, D., and Schonbrunner, E. Klin. Wschr. 1937, 16: 340–344.
28. Schweitzer, A. J. Physiol., 1936, 87: 46P–48P.
29. Schwiegk, H. Arch. ges. Physiol., 1935, 236: 206–219.

THE NATURE OF LATERAL "ABERRANT" THYROID TUMORS

SHIELDS WARREN, M.D., and J. D. FELDMAN, M.D., Boston, Massachusetts

A CONTROVERSY has existed for many years concerning tumors of thyroid tissue in the lateral regions of the neck. In the earliest reports of these tumors the opinion was held that they represented neoplasia of aberrant thyroid tissue. But the association of lateral cervical tumors with neoplasm of similar structure within the thyroid gland, in many if not in all the cases, has recently led to the opinion that they represent secondary rather than primary growths. From the evidence adduced at the present time it is clear that lateral thyroid tumors must be appraised in relation to tumors of the main thyroid gland. There are three possibilities to consider: (1) lateral thyroid tumors originate in thyroid tissue which is separated from the thyroid gland by defective embryogenesis and in the majority of cases metastasize to the thyroid; (2) tumors in thyroid and aberrant thyroid tissue represent multicentric neoplastic growth in a single type of embryonal rest; (3) they are early metastases from a tumor of the thyroid gland and become clinically apparent before the tumor of the thyroid manifests itself.

It is the purpose of this paper to determine what features connected with the growth of these tumors can be considered as evidence for one or another mode of origin. For this purpose we shall present an analysis of all the lateral thyroid tumors received in the laboratory of the New England Deaconess Hospital[1] over a period of 19 years.

MATERIAL

There were 63 cases diagnosed as lateral aberrant thyroid tumor among approximately 20,000 surgically removed thyroids, in a 19 year period, an incidence of slightly more than 0.3 per cent. This series also represents 3.9 per cent of 1,610 benign and malignant thyroid tumors in the surgical material. Selection of cases was determined by the clinical or pathological diagnosis. The clinical diagnosis was made on the observation that a lateral mass, or masses, was palpable while the thyroid gland was and remained clinically negative; that the lateral mass was larger than any nodule felt in the thyroid gland; or lastly, that a cervical mass was present before the thyroid was noticeably affected. Occasionally the diagnosis was based on the microscopic findings by the pathology department.

In 57 cases the clinical diagnosis of lateral thyroid tumor was confirmed by the histological examination. There were 6 remaining cases which were not confirmed by microscopy. Of these latter 2 were metastatic tumors unrelated to thyroid tissue; they were single nodules of cancer present in the lateral side of the neck. In 4 cases colloid adenomatous thyroid tissue unconnected with the thyroid gland was present. Two of these patients had been operated upon elsewhere, 2½ and 30 years previously, following which adenomatous tissue developed in an aberrant site. A third had cancer of the lung, for which a biopsy of a single cervical nodule was performed and this proved to be colloid adenomatous thyroid tissue. His thyroid was not investigated. The fourth was a woman with goiter of 17 years' duration who had a small mass in the left supraclavicular area near to, but unconnected with, an enlarged non-neoplastic adenomatous left lobe.

The observations to be made in the following are concerned primarily with the 57 cases.

OBSERVATIONS

Clinical. Table I shows the age distribution of the series.

The data reveal a predominance of women in a ratio of a little more than 2 to 1 with an

From the Laboratory of Pathology, New England Deaconess and New England Baptist Hospitals and the Harvard Cancer Commission.

[1]Most of the surgical material reported in this paper comes from the surgical service of the Lahey Clinic.

TABLE I.—AGE DISTRIBUTION

Age years	No. cases
1–10	2
11–20	3
21–30	20
31–40	13
41–50	11
51–60	7
61–70	1

Females 39 Males 18
Range 7–62 years

TABLE II.—DURATION OF HISTORY BEFORE TREATMENT AT THIS HOSPITAL

Years	No. cases
Less than 1	13
1– 2	15
3– 5	8
6–10	12
11–15	2
Over 15	1
Not stated	6

average at admission for the entire series, of 34.7 years. In the general thyroid material at this institution the ratio of women to men is 4:1 and the average age at admission of the surgical thyroid patient is 43.0 years, 7½ years more than the average of this series. Almost two-thirds of the patients of this series are below the age of 40.

Table II presents the pretreatment interval. Here it is worthy of mention that a patient waited on the average almost 4 years (average duration 3.9 years) before seeking treatment and that 3 patients had histories of over 10 years. No correlation between the age of the patient and the duration of the history was disclosed.

The majority of patients had but one complaint, a lump, nodule, or swelling in the neck which gradually enlarged. Forty-three of the 57 patients offered this as a primary symptom and of these 37 had no other symptoms. In 4 instances the presence of a cervical mass was not noted by the patient and was discovered by the examining physician. Other symptoms consisted of a pressing or choking sensation, fatigue, dyspnea, local pain, or tenderness. Signs rarely found were weight loss and voice change. When secondary symptoms and signs were present they usually occurred several weeks or months before the patient sought medical aid and were effective in forcing patient to find relief.

TABLE III.—CLASSIFICATION OF LATERAL MASSES CLINICALLY REGARDED AS ABERRANT THYROID

Tumor masses not identifiable as nodes	Nodes containing tumor	Negative nodes
1	—	—
1	—	—
1	—	—
1	—	—
2	—	—
2	—	—
2	—	—
2	—	—
3	—	—
4	—	—
4	—	—
6	—	—
6	—	—
2	1	—
1	2	—
2	2	—
4	4	—
1	1	2
2	1	3
2	3	1
2	1	4
2	1	5
2	3	3
3	3	5
4	3	6
6	4	1
–	1	—
–	1	—
–	5	—
–	11	—
1	—	1
1	—	1
1	—	2
2	—	1
2	—	1
2	—	1
1	—	4
1	—	5
2	—	4
4	—	3
6	—	11
–	3	1
–	3	6
–	4	6
–	10	3
–	2	19

BILATERAL CERVICAL MASSES

	Tumor masses not identifiable as nodes	Nodes containing tumor	Negative nodes
Right	1	—	—
Left	1	—	—
Right	1	—	—
Left	1	—	—
Right	1	—	—
Left	1	—	—
Right	4	—	—
Left	8	—	—
Right	–	2	3
Left	–	4	1
Right	3	2	1
Left	3	2	—

TABLE III.—*Continued*

	Tumor masses not identifiable as nodes	Nodes containing tumor	Negative nodes
Right	7	1	6
Left	2	—	4
Not separated as to side	–	—	8

None of the patients had thyrotoxicosis. Two patients at the time of hospital entry had an elevated basal metabolic rate but displayed no other objective manifestations of a hyperfunctioning thyroid.

The lateral cervical masses. The lateral cervical masses which were excised and which were regarded clinically as aberrant thyroid tumors turned out to be one or more of the following: (1) neoplasm of thyroid tissue; (2) lymph node or nodes partially replaced by tumor; (3) negative lymph nodes. The histologic criteria of lymph nodes, especially those that were almost completely replaced by tumor, were a fibrous capsule, peripheral lymphoid follicles with germinal centers, and sinuses (Figs. 1, 2, 3). This combination of capsule, follicles, and sinuses was not seen in any of the tumors of the thyroid gland nor has it been found in other diseased thyroids except Hashimoto's struma along the capsular margin of the gland.

There were 17 cases in which the lateral masses microscopically consisted only of tumor. In these instances the extirpated tumors showed no evidence of nodal structure in any portion nor was there any evidence as to their source, i.e., whether they arose from embryonal rests or from negative thyroid tissue. The number isolated in the laboratory ranged from 1 to 12 (Table III). In short, if the lateral tumors in these cases originated from defective embryogenesis or from a metastasis from the thyroid, there were no histologic findings to prove either derivation.

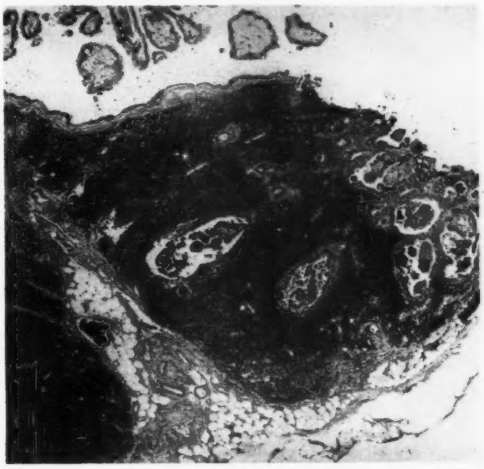


Fig. 1. Lymph node partially replaced by tumor. ×30.

In 4 cases the lateral masses consisted of

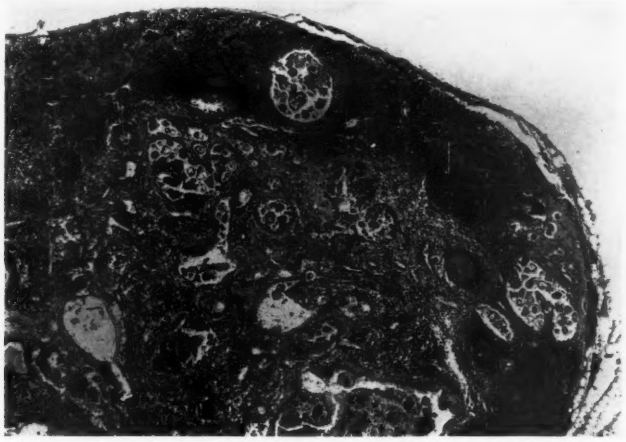


Fig. 2. Lymph node partially replaced by tumor. ×20.

Fig. 3. Lymph node with lymphatic invasion by tumor. ×120.

both tumor masses and lymph nodes containing tumor. There were 12 cases in which the cervical masses were tumor nodules, lymph nodes partially replaced by tumor, and negative lymph nodes. There were 4 cases in which the masses were only lymph nodes containing tumor; 14 cases in which the masses were both tumor and negative lymph nodes; 4 cases in which the masses were lymph nodes, either partially replaced by tumor or uninvolved; and 1 case in which the masses received in the laboratory were merely negative lymph nodes. This last patient had had a previous operation elsewhere with removal of a lateral mass and the diagnosis of thyroid neoplasm was confirmed in this laboratory by examination of the slides (Case 5).

Table III is a tabulation of these data and shows the pathology of the lateral cervical masses.

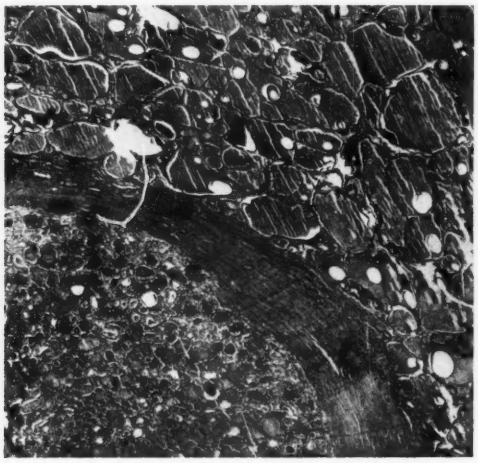


Fig. 4. Nodule of adenocarcinoma in thyroid gland. ×30.

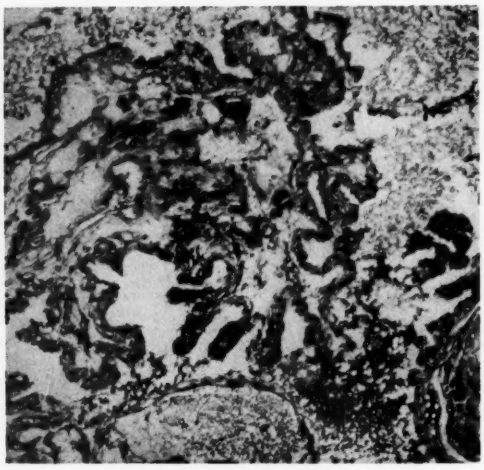


Fig. 5. Malignant papillary cystadenoma in lateral cervical mass. Same case as shown in Figure 4. ×75.

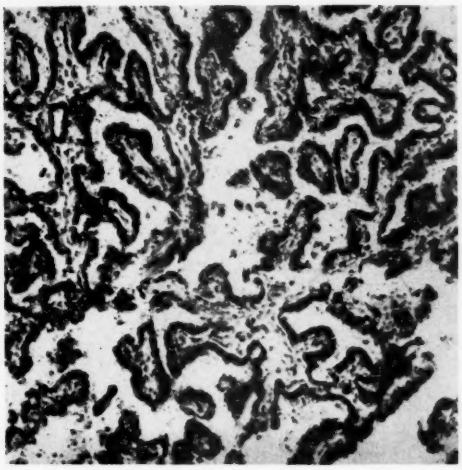


Fig. 6. Papillary area of thyroid tumor. ×75.

Table III reveals that in 45 of the 57 cases some of the lateral cervical masses were lymph nodes, either uninvolved or containing tumor. It was apparent, also, when the material was examined microscopically, that there were many cases in which gradations existed ranging from negative lymph nodes, to partially replaced nodes, to masses which could not be certainly recognized as nodal tissue.

The average number of lateral masses was six. Their size ranged from 0.5 centimeter in diameter to 8 centimeters in diameter, most being about 1.5 centimeters in diameter. There was no correlation between the number and size of tumor masses or lymph nodes containing tumor and their duration in the neck as disclosed by history.

The location of the cervical masses was variable and widespread. They were seen most often as a chain extending from mastoid process to clavicle, but they were also anterior to the sternocleidomastoid muscle, posterior to the sternocleidomastoid muscle, lateral to the great vessels of the neck, in the submaxillary triangle, substernally, and at the angle of the jaw as a single tumor. They were on the right side 23 times, on the left side 23 times, bilateral 8 times, and position not stated 3 times.

In the 57 cases studied histologically the diagnoses were as follows: malignant papillary cystadenoma, in 33; adenocarcinoma, in 14; papillary adenocarcinoma, in 6; and carcinoma simplex in 4.

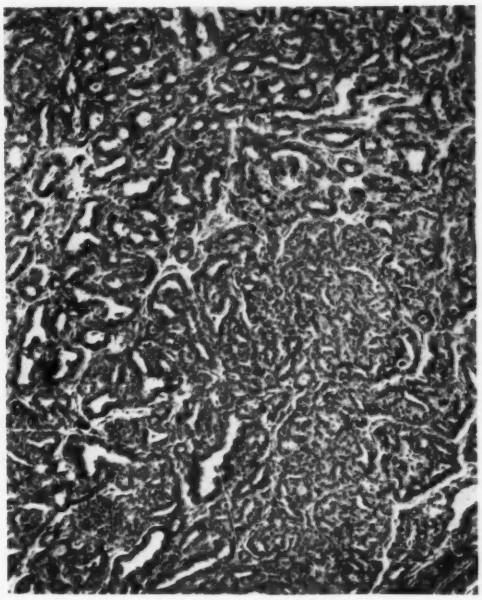


Fig. 7. Area of adenocarcinoma of thyroid tumor. Same case as shown in Figure 6. ×75.

The thyroid gland. In 49 cases, the thyroid gland contained a tumor. In every instance

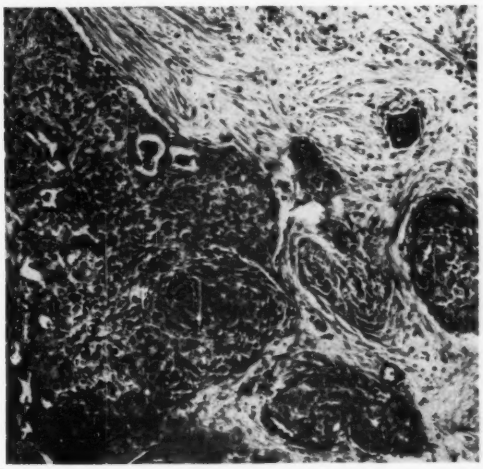


Fig. 8. Area of carcinoma simplex of thyroid tumor. Same case as shown in Figures 6 and 7. ×75.

Fig. 9. Typical malignant papillary cystadenoma. ×20.

the thyroid neoplasm was malignant and in all but 1 case was histologically identical with the lateral masses. In this latter patient there was an adenocarcinoma of the thyroid gland while the cervical masses presented a malignant papillary cystadenoma (Figs. 4 and 5).

There were 8 cases of the 57 in which a cancer of the thyroid was not found. Of these, the glands of 4 patients were not removed, having been regarded as negative at operation. In the remaining 4 cases the thyroids had been previously removed elsewhere and were not available for study.

Almost 15 per cent of the series were clinically free of thyroid disease though neoplasm was revealed at operation or in the laboratory. At the physical examination the thyroid was stated to be negative in 5 instances, yet at operation a neoplasm was found larger than 1 centimeter in diameter. In 3 cases the gland was neither mentioned nor described in the history and a tumor was disclosed at operation. There was 1 case in which the thyroid after palpation at operation was stated to be negative. A tumor, however, less than 0.5 centimeter in diameter, was discovered in the pathological laboratory. This was the only time a tumor was found in the thyroid less than 1 centimeter in diameter.

Precise anatomical location of the neoplasm in the thyroid was described in 18 cases. A superior pole alone was involved in 7 cases. An inferior pole alone was involved in 5 cases. A single discrete nodule was present in both lobes or in one lobe and the isthmus in 4 instances. And in 1 patient there were two distinct tumor nodules in a single lobe. The remaining 31 patients were either not examined for location of the neoplasm or were diffusely affected throughout one or both lobes.

A comparison between the size of the thyroid tumor and the size of the lateral masses could not be made, for in many instances the thyroid malignancy was not carefully measured. There were, nevertheless, at least 2 cases in which a single cervical mass was known to be larger than the tumor in the thyroid. In 41 cases in which there was a neoplasm of one lobe, the affected lobe and the lateral cervical masses were on the same side. There were 7 instances in which both lobes contained a neoplasm and 1 instance in which a lobe and the isthmus were involved. In these latter cases there were bilateral cervical masses present.

Histology. The histology of the lateral masses and thyroid tumors was quite pleomorphic, but except for 1 case the neoplasms in the thyroid gland and the lateral masses were histologically identical. Table IV lists the microscopic classification of the tumors, including the 8 cases in which only the lateral masses were available.

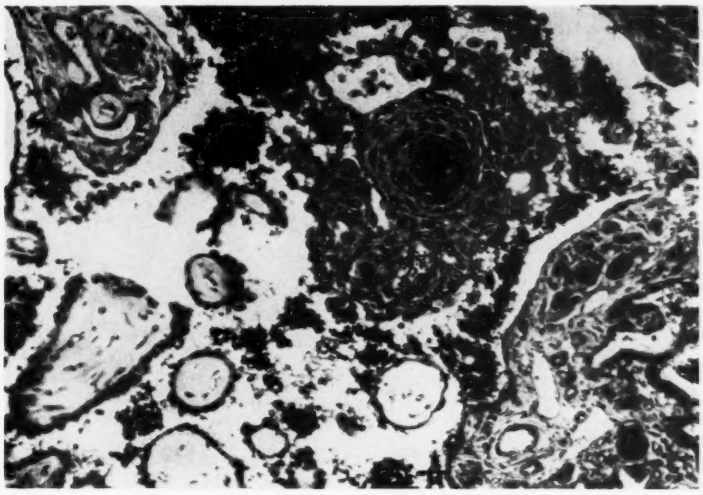


Fig. 10. Squamous metaplasia in malignant papillary cystadenoma. ×120.

These diagnoses were based on the predominant pattern of growth revealed in microscopic section. The patterns were markedly variable (Figs. 6, 7, 8). In almost every instance individual microscopic fields could be found which showed negative-appearing follicles, fetal thyroid tissue, complex arborescent fronds, adenocarcinoma and carcinoma simplex. Generally, however, a single pattern predominated and this was usually of a papillary nature (Figs. 9 and 10). Thirteen of the 14 cases of adenocarcinoma exhibited scattered minute regions of papillary structure. For the most part the neoplasms were well differentiated, showing slight to moderate neoplasia and rare mitoses. Calcific concretions were seen 53 times, being present in all tumors of the first three classifications. Ossification was present in 1 malignant papillary cystadenoma (Fig. 11). In 2 instances the neoplastic tissue deviated so little cytologically from the normal that malignancy would not be suspected except for the fact that thyroid acini formed tumor emboli in one (Fig. 12), and were in the corium of the skin in the other case.

The cytological changes of malignancy were frequently difficult to evaluate, for epithelial alteration was often slight. But generally the epithelium showed definite recognizable differences from the epithelium of normal, hyperplastic, or nodular goitrous thyroid. When found, the changes were the same as those which characterize malignancy anywhere else in the body.

More obvious than the cytologic changes were the invasive properties. The latter included blood vessel, lymphatic, and invasion of surrounding tissue. True intravascular invasion was accepted only if thyroid epithelium formed part of a thrombus or embolus within a fibromuscular wall lined with endothelium and having an elastic lamina, or if the

TABLE IV.—MICROSCOPIC CLASSIFICATION

	Lateral masses and thyroid	Lateral masses only
Malignant papillary cystadenoma	29	4
Adenocarcinoma	11	3
Papillary adenocarcinoma	5	1
Carcinoma simplex	4	0

TABLE V.—TYPES OF INVASION

	Papillary cyst-adenoma	Adeno-carcinoma	Papillary adeno-carcinoma	Carci-noma simplex
Blood vessel invasion, with or without lymphatic or simple invasion	12	10	4	4
Lymphatic invasion with or without simple invasion	6	2	0	0
Invasion of adjacent tissue	10	0	1	0

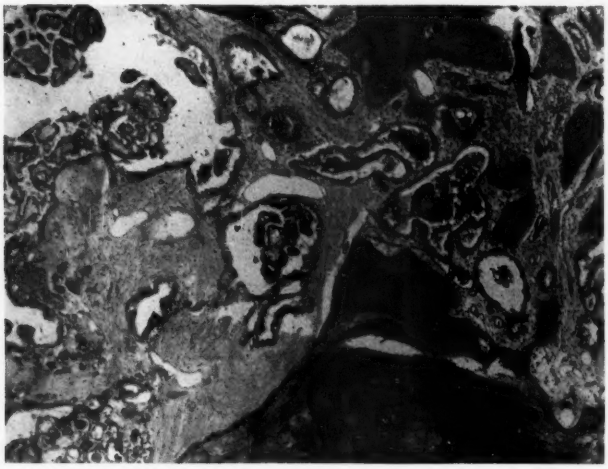


Fig. 11. Ossification in malignant papillary cystadenoma. ×30.

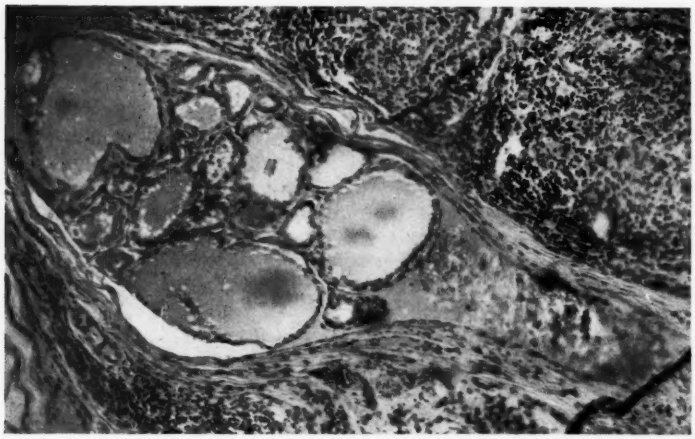


Fig. 12. Blood vessel invasion. Note negative appearing thyroid follicles and lack of cytological alteration. ×75.

epithelium was attached to such a wall (Fig. 13). Lymphatic invasion was represented by the presence of tumor within at least three endothelial-lined spaces at a distance from the cut edge of the section (Fig. 14). Invasion of adjacent tissue was considered present if there was actual infiltration of capsule, of negative-appearing thyroid parenchyma, or of both (Fig. 15).

With these criteria it was found that the 49 cases in which the thyroid was available showed one or more of the above invasive properties in the sections taken from the thyroid tumor. Occasionally the lateral neoplasms of these cases exhibited intravascular or lymphatic infiltration but this was noted less frequently than in the material from the thyroid gland. The data are given in Table V.

There were 8 patients from whom only the lateral cervical masses were resected. The thyroid was removed elsewhere in 4 instances and in 4 instances no resection was done be-

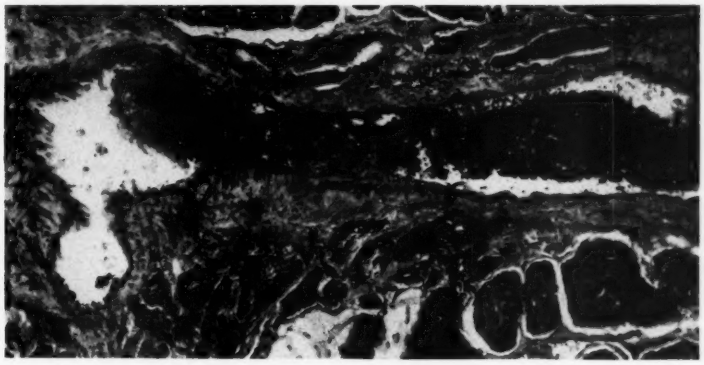


Fig. 13. Blood vessel invasion. ×75.

cause the gland was negative at operation. In 5 of these 8 cases the lateral masses showed invasive characteristics and were either lymph nodes partially replaced or solely tumor tissue not identifiable as being in lymph nodes. In 2 cases no invasive features were exhibited and the masses consisted entirely of neoplastic tissue. In the last case the cervical masses were 8 negative lymph nodes, no tumor being present (Case 5).

Outcome. Follow-up observations are not available for most of the patients. For 9 there are partial data concerning outcome of treatment. Of these there were local recurrences in 8 patients with subsequent death of 1. The ninth patient, with a malignant papillary cystadenoma, was admitted to the hospital for cardiovascular renal disease 10 years after a radical neck dissection. At this time he was clinically free of thyroid malignancy. The patient who died suffered four local recurrences over a period of 11 years and finally succumbed following a craniotomy for removal of thyroid metastases to skull and brain (Fig. 16). Her tumor at first cytologically resembled negative-appearing thyroid tissue (mentioned before

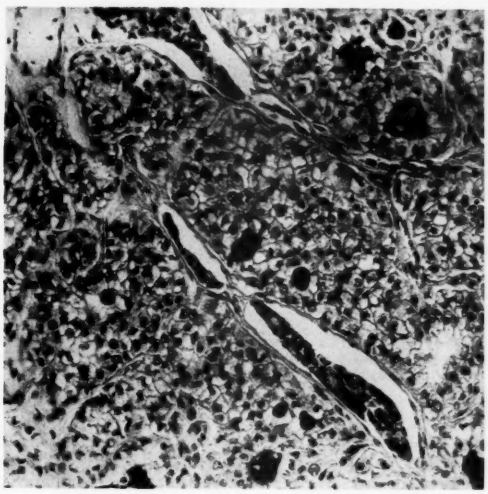


Fig. 14. Lymphatic invasion present at a distance from cut edge of the section. ×180.

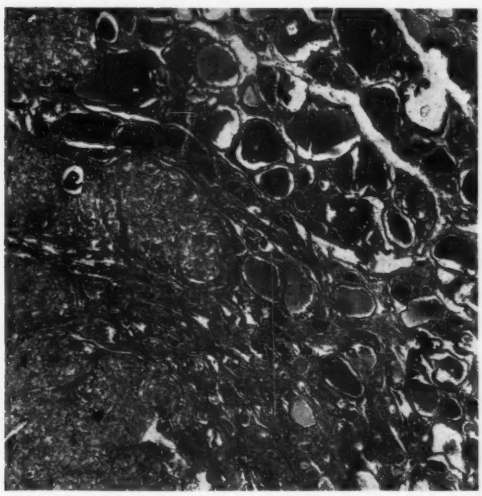


Fig. 15. Simple invasion of thyroid gland by tumor. ×30.

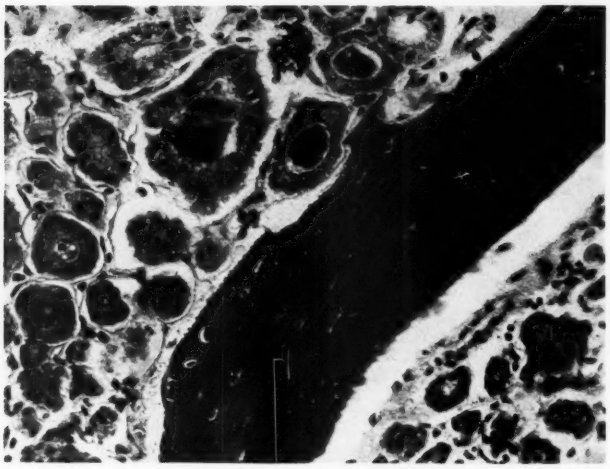


Fig. 16. Metastasis of thyroid carcinoma to skull bone. ×245.

under histology), but it later assumed, in the course of her disease, the histologic features of an adenocarcinoma. One patient with a malignant papillary cystadenoma suffered a recurrence 1⅔ years after her operation. Another with the same type of neoplasm experienced 2 recurrences over a 2 year period. One patient with an adenocarcinoma had a local recurrence after 1⅔ years. A second with the same type of tumor had a recurrence 2 years after surgical treatment. A third patient with an adenocarcinoma suffered a recurrence 7½ years following her first operation. There was a papillary adenocarcinoma which recurred twice over a 6⅔ year period. The last patient with a carcinoma simplex experienced 3 recurrences over a 14 year period. The final status of these 7 patients is unknown.

TABLE VI

Type of tumor	No. of recurrences or metastasis	Time interval years	Site of recurrence or metastasis
Malignant papillary	1	1⅔	Neck; on same side as thyroid tumor
Cystadenoma	1	2	Neck; on side opposite to thyroid tumor
	0	10	
Adenocarcinoma	1	1⅔	Neck; same side as thyroid tumor
	1	2	Neck; same side as thyroid tumor
	1	7½	Neck; same side as thyroid tumor
	5	11	1st 2 recurrences in neck on side opposite to original tumor; 3rd and 4th recurrences in neck bilaterally; 5th recurrence in skull as metastasis
Papillary adenocarcinoma	2	2	Neck; both on side opposite to thyroid tumor
Carcinoma simplex	3	14	1st recurrence in neck, side opposite to original tumor; 2nd recurrence in neck, on same side as original tumor; 3rd recurrence infiltration of trachea

ILLUSTRATIVE CASE REPORTS

CASE 1. *Typical case.* A 23 year old woman had a slowly enlarging mass in the right side of her neck for 10 years. There were no other symptoms. Examination disclosed a 2 by 4 centimeter nodule in the right neck, anterior to the sternocleidomastoid muscle just above the level of the thyroid. The thyroid was negative to palpation. At operation several masses were found in the right neck and the right lobe of the thyroid was the site of malignant change. A block dissection was done. In the laboratory a malignant papillary cystadenoma of the thyroid was found microscopically. There were also 7 lymph nodes isolated, including the nodule described. Two of these were partially replaced by the same type of neoplasm.

CASE 2. *Local recurrences.* A 34 year old woman noticed a mass in left side of her neck for 3 years which fluctuated in size. Two months before admission she experienced a choking spell and was found to have a recurrent laryngeal nerve paralysis. A biopsy

elsewhere from one of the cervical masses revealed thyroid adenocarcinoma. At operation numerous "aberrant" nodules were present on both sides of the neck, extending from the upper neck into the mediastinum. The entire thyroid was diffusely enlarged. "Aberrant" tissue had invaded the carotid sheath and pretracheal fascia. In two stages a left total hemithyroidectomy and radical dissection of left side of neck was done followed by a right total hemithyroidectomy and partial neck dissection. Microscopically there was a well differentiated adenocarcinoma in the thyroid. Of 5 nodules isolated from the right side, 4 were lymph nodes partially replaced by cancer and the fifth was composed entirely of tumor tissue. Of 5 nodules isolated from the left side 3 were negative lymph nodes and 2 contained metastases. Blood vessel, lymphatic, and stromal invasion were marked.

Twenty months later, after several series of x-ray treatments, the patient was reoperated upon because of recurrence about the trachea. Eight months after this procedure she was treated with surgery for a third time because of local recurrence. Microscopic sections of tissue removed at these operations revealed the same tumor as was originally seen. The final status of the patient is unknown.

CASE 3. *Data insufficient for final diagnosis.* A 43 year old woman was admitted to the hospital because of a lump in her neck. Seven years before she had had a left hemithyroidectomy for Graves' disease and 5 years before had a partial thyroidectomy also because of thyrotoxicosis. Four years after the second operation a nodule developed in her neck, which proved to be thyroid tissue. Two months before admission a second mass appeared to the right of the thyroid cartilage. There were no other symptoms. At operation numerous nodules were found about the right internal jugular vein which had to be divided. The thyroid region was not examined. Pathological reports on the tissue previously removed were not available. At the present pathological examination 11 nodules were isolated. Of these one was a negative lymph node; 4 were nodes partially invaded by thyroid neoplasm; and the remaining were thyroid neoplastic tissue not identifiable as lymph nodes. Histologically the tumor was pleomorphic but predominantly a malignant papillary cystadenoma.

CASE 4. *True ectopic thyroid.* A 49 year old woman had a thyroidectomy 30 years ago, 11 years after the operation a lump appeared in right side of neck and slowly enlarged. There were no other symptoms. At operation, 19 years after the appearance of the cervical mass, a tumor 2 centimeters in diameter was located beneath the skin just at the tip of the old scar. The thyroid remnants on the right side were negative to palpation. Microscopically the excised tissue showed the histology of a fetal adenoma, completely encapsulated and exhibiting no evidence of invasiveness or cytologic malignancy.

CASE 5. *Tumor of thyroid and lateral cervical mass removed elsewhere.* A 7 year old boy was operated upon at another hospital where an encapsulated mass was excised from the thyroid gland and another mass removed from the left side of the neck. The microscopic diagnosis was adenocarcinoma, which was confirmed by Dr. Shields Warren. Two months later he was admitted to this institution for an exploration of his neck, and for advice as to future management. At operation the thyroid appeared to be negative. Eight small nodules, located along the course of the internal jugular vein bilaterally and thought to be aberrant thyroid tissue, were excised. The thyroid was not removed. Microscopically the 8 nodules were lymph nodes.

DISCUSSION

Numerous pitfalls beset the study of "aberrant" thyroid tissue. First, it is obvious that many of the early case reports were incomplete (1, 9, 23, 24, 26, 29, 33, 35). Excision of lateral masses was accomplished without inspection or palpation of the thyroid before or during operation. Furthermore, clinical and operative examinations of the gland were often inadequate. In this series almost 15 per cent of the cancers of the thyroid gland were not palpated before operation and one was missed during the surgical procedure, only to be discovered in the laboratory. In more recent years, as the thyroid has been examined more closely or removed at operation for "lateral aberrant thyroids," more and more neoplasms have been found (2, 3, 4, 7, 10, 12, 19, 22, 37). Crile has particularly pointed out that thyroid cancer was occasionally not perceived until the gland was lifted from its bed and its posterior surface studied (8).

A second pitfall exists because of the confusion between lateral thyroid neoplasms, as observed in this paper, and ectopic fragments of thyroid tissue found occasionally at autopsy or rarely during thyroidectomies. The latter masses are not true tumors and are of two types. One type is an encapsulated fragment of tissue, usually measuring between 3 to 5 millimeters in diameter, which, though completely separated from the gland, is directly contiguous with the capsule. Histologically it is composed of a normal thyroid architecture. Other larger masses comprise the second type, are found in the mediastinum or supraclavicular regions, and are associated with enlarged adenomatous thyroids which have endured longstanding disease. Histologically these show

a colloid adenomatous structure. Pemberton suggests they are pinched off from the thyroid gland by scarring (18). Four such cases were mentioned early in this paper but were not included in the analysis because they did not form true tumors in the lateral aspects of the neck.

A third pitfall is related to the peculiarities of thyroid tissue, biologically and cytologically. The patterns of growth in diseased glands are amazingly variable and especially is this true for the low grade thyroid malignancies. Graham demonstrated long ago that portions of thyroid cancers can mimic microscopically the entire gamut of cellular change found in non-neoplastic disease (13, 14). He insisted, and this series reaffirms it, that the important signs of malignancy are the invasive features. Since morphologic alteration is so slight, pathologists in the past have often not recognized thyroid cancer. Biologically, also, the low-grade thyroid cancers, especially those with papillary structures, are slow-growing and tend to cause death late. Numerous documented case reports, only now being described in the medical literature, attest to this phenomenon (5, 8, 12, 18). The growth and expansion of these tumors should more often be measured in decades rather than years. Moreover, metastases may outgrow in size the original tumor and may proliferate for long periods before causing death. Previous to 10 years ago the reported cases were insufficiently followed and the complete history of them had not been traced to the end.

A final pitfall of the subject is concerned with lymphoid tissue. Thyroid glands diseased for long periods of time, be they of the hyperplastic or nontoxic adenomatous types, tend to accumulate lymphoid tissue and even well formed follicles. In addition, embryologists have noted the development of lymphoid aggregates about differentiating cell clusters derived from various branchial pouches. Hence, many authors feel that the presence of lymphoid tissue in and around thyroid tissue does not signify a lymph node. But lymphoid stroma in diseased thyroids do not reduplicate the architecture of a node, for sinuses are lacking. The histologic picture of thyroid neoplasm surrounded partly or wholly by a fibrous capsule, a row of follicles with germinal centers and sinuses can usually be recognized as a metastasis to a lymph node. Rarely is the combination of capsule, follicles, and sinuses found in diseased thyroids, and then only in Hashimoto's struma.

After anatomists noted ectopic thyroid nodules in the neck (15, 16) and after embryologists described the genesis of the gland (17), it was an easy and logical step to postulate a theory of embryonal rests. To this assumption there have been several additions. Schrager hypothesized that the embryonal rests were "inferior" thyroid tissue and that they enlarged when demands upon the thyroid became excessive. Others felt that embryonal rests were prone to become neoplastic and then metastasize to the thyroid and regional lymph nodes (2, 3, 12, 22). Cohn and Stewart, in order to explain the presence of tumor in the thyroid gland as well as in the lateral neck, theorized that in some cases the lateral primordium retained its identity after fusion with median anlage of the fetal thyroid.

These theories are inadequate to explain the many facets of the problem. First, it is agreed among embryologists that cell aggregates from the fourth branchial pouch fuse with the median anlage of the fetal thyroid. Beyond this there is no agreement. Kingsbury maintained that the lateral primordia degenerated after fusion (20, 21), while Norris and Weller stated that the fourth pouch contributed functioning thyroid follicles to the gland (27, 28, 36). Second, there is no morphological or physiological evidence for "inferior" thyroid tissue. "Lateral aberrant thyroid" tissue is neoplastic and does not resemble normal, hyperplastic, or adenomatous thyroid tissue. Nor do patients with cervical masses of thyroid tissue exhibit thyrotoxicosis to suggest increased stress upon the thyroid. Third, Mahorner and associates have demonstrated that the lymphatics of the thyroid carry away from the organ. Fourth, if it is conceded that the lateral primordia form functioning thyroid tissue, and if Norris and Weller are correct in stating that they form the upper poles of the two lobes, then neoplasms in the gland, derived from rests, should arise in the upper poles. In the present series cancer was present in the in-

ferior pole alone at least five times and in the isthmus once.

If "lateral aberrant thyroids" are a result of defective embryogenesis, then occasionally, at least, thyroid remnants and tumors should be found in branchial cleft cysts which represent anomalous development of one or more branchial pouches. Among 113 branchial cleft cysts operated on in this institution, only 3 tumors were found and none of these was composed of thyroid tissue. Crile and Kearns discovered only epidermoid carcinoma in 28 branchial tumors (6). Nor are remnants of thyroid tissue seen in branchial cleft defects.

On the other hand, median aberrant thyroid tissue is often associated with thyroglossal duct cysts (30). The thyroglossal duct is derived from the development of the median anlage, which grows out of the pharyngeal pouch. Collections of thyroid acini were present 77 times among 190 patients operated upon here for this fetal anomaly (11). It is noteworthy that "lateral aberrant" thyroid tumors have not shown similar clusters of thyroid acini nor have the lateral neoplasms been discovered developing from such thyroid follicles.

As for the distribution of the cervical masses, it is too widespread to be contained within the tract of the migrating fourth pouch. The lateral tumors have been found external to the carotid artery, substernally, at the mastoid process and in the submaxillary triangle, sites which are beyond the anatomic wanderings of the primordial lateral thyroid.

Finally there is a marked similarity between the so-called lateral aberrant thyroid tumors and the malignant papillary cystadenomas of the thyroid gland. They resemble each other in age and sex distribution, in length of the pretreatment interval, in their histology, biology and final outcome. An analysis of 120 malignant papillary cystadenomas in our laboratory revealed no essential difference from the lateral "aberrant" tumors, with the one exception that the latter were discovered clinically before the presence of a cancer in the thyroid was noted (11). A comparison with Pemberton's data on papillary carcinomas of the thyroid also disclosed the similarity between the lateral cervical tumors and papillary neoplasms. His and our data show that the histological, biological, and clinical features of the two groups are the same (31, 32).

Our data indicate that lateral thyroid tumors of the neck are metastases from cancers of the thyroid. This is supported by the following: (1) all thyroid glands received in the laboratory contained a tumor which was histologically identical with the neoplasms in the lateral neck; (2) in the majority of cases some of the lateral masses, clinically regarded as aberrant thyroid tissue, were either lymph nodes partially replaced by tumor or uninvolved; (3) the distribution in the neck of the lateral masses was the same as the anatomical disposition of cervical lymph nodes; (4) the characteristics of these lateral tumors were the same as the low-grade papillary carcinomas of the thyroid; (5) study of branchial cleft cysts and thyroglossal ducts, embryologic anomalies associated with thyroid development, revealed no evidence that lateral "aberrant" thyroid tumors develop from embryonal rests.

SUMMARY

1. An analysis was made in 57 cases clinically diagnosed lateral "aberrant" thyroid tumors. Six other cases were not included because they proved not to be tumors on histologic examination.

2. In 49 of the 57 cases there was an associated thyroid cancer; 15 per cent of these were not detected clinically. In the remaining 8 cases the thyroid gland was not received in the laboratory, either because they were removed elsewhere or because they were regarded as uninvolved by tumor at operation.

3. The histology of the tumor in the thyroid and in the lateral masses of the neck was identical in all but 1 instance. It was usually papillary in structure, though the neoplastic growth patterns were markedly pleomorphic.

4. In 40 of the 57 cases the lateral tumors were found to be metastases to cervical lymph nodes. In the remaining 17 cases there was no microscopic evidence that the lateral tumors were either metastatic or derived from embryonal rests.

5. These neoplasms tend to occur in a younger age group than does cancer in general

or than does thyroid disease. The presenting finding is usually only a swelling or nodule in the neck, with an average pretreatment interval of almost 4 years.

6. The disease often recurs locally unless completely eradicated by surgery. Follow-up observations must be made over decades rather than years.

7. The data indicate that most if not all lateral thyroid tumors of the neck are metastases from cancers of the thyroid.

REFERENCES

1. Billings, A. E., and Paul, J. R. Bull. Ayer Clin. Lab., 1925, 9: 27–44.
2. Cattell, R. B. J. Am. M. Ass., 1931, 97: 1761–68.
3. Idem. Tr. Am. Ass. Goiter, 1940, pp. 218–21.
4. Clay, R. C., and Blackman, S. S., Jr. Arch. Surg., 1944, 48: 223–38.
5. Cohn, L. C., and Stewart, G. A. Arch. Surg., 1940, 40: 585–605.
6. Crile, G. S., and Kearns, J. E., Jr. Surg. Gyn. Obst., 1935, 60: 703–709.
7. Crile, G., Jr. Surg. Gyn. Obst., 1939, 69: 39–47.
8. Ibid., 1947, 85: 757–766.
9. Dunhill, R. P. Brit. J. Surg., 1931–1932, 19: 83–113.
10. Eberts, E. M. Canad. M. Ass. J., 1933, 28: 32–33.
11. Feldman, J. D. Unpublished data.
12. Frantz, V. K., Forsythe, R., Hanford, J. M., and Rogers, W. M. Ann. Surg., 1942, 115: 161–83.
13. Graham, A. Surg. Gyn. Obst., 1924, 39: 781–790.
14. Idem. Ann. Surg., 1935, 82: 30–44.
15. Gruber, W. Virchow's Arch., 1876, 66: 447–54.
16. von Haller. Quoted by Schrager (34).
17. His, W. Anatomie menshlichen Embryonen. Leipzig, 1885.
18. Kennedy, R. L. J. Pediat., 1935, 7: 631–50.
19. King, W. L., and Pemberton, J. deJ. Surg. Gyn. Obst., 1942, 74: 991.
20. Kingsbury, B. F. Anat. Rec., 1934–1935, 61: 155–174.
21. Idem. Am. J. Anat., 1939, 65: 333–360.
22. Lahey, F. H., and Ficarra, B. J. Surg. Gyn. Obst., 1946, 82: 705–711.
23. Lawton, S. E. Surg. Gyn. Obst., 1946, 56: 696.
24. Leech, J. F., Smith, L. W., and Clute, H. M. Am. J. Path., 1928, 4: 481–492.
25. Mahorner, H. R., Caylor, H. D., Schlotthauer, C. F., and Pemberton, J. deJ. Anat. Rec., 1927, 36: 341–348.
26. Moritz, A. R., and Bayless, F. Arch. Surg., 1932, 24: 1028–1043.
27. Norris, E. H. Am. J. Anat., 1918, 24: 443–465.
28. Idem. Contr. Embryol. Carnegie Inst., 1937, 26: 242–294.
29. Paget, J. Lectures on Surgical Pathology. Vol. II. London: Longman, Brown, Green, and Longmans, 1853.
30. Patterson, N. J. Lar. Otol., Lond., 1928, 43: 313–328.
31. Pemberton, J. deJ. Ann. Surg., 1934, 100: 906–923.
32. Idem. Surg. Gyn. Obst., 1939, 69: 417–430.
33. Rouroff, A. S. W. Ann. Surg., 1941, 113: 73–76.
34. Schrager, V. L. Surg. Gyn. Obst., 1906, 3: 465–475.
35. Smith, M. K. Ann. Surg., 1941, 113: 77–81.
36. Weller, G. L., Jr. Contr. Embryol., 1937, 24: 93–139.
37. Wohl, M. G. Interstate M. J., 1917, 24: 1044–1049.

EVALUATION OF SKIN GRAFTING IN THE TECHNIQUE OF RADICAL MASTECTOMY IN RELATION TO LOCAL RECURRENCE OF CARCINOMA

HERBERT CONWAY, M.D., and CHARLES G. NEUMANN, M.D., New York, New York

THE percentage of patients alive and free from recurrence or metastasis 5 years after operation is the common measure of the effectiveness of radical mastectomy in the treatment of carcinoma of the breast. In the course of the years since the Halsted technique of radical mastectomy was established, the percentage of 5 year "cures" has increased progressively. Although the basic principles of the technique of operation as developed by Halsted are in use in many clinics throughout this country, certain variations have been developed. These variations concern the type of incision and the amount of mammary skin which is removed. While subcutaneous tissues and musculature may be excised freely from the thoracic area, the necessity for wound closure restrains the surgeon in the excision of wide margins of skin. The introduction by Halsted of the use of skin grafting made radical excision of skin a more feasible step. Still there is active dispute concerning the amount of skin which should be removed in conjunction with a given tumor. The opinion has been expressed that only by wider excision of skin can local recurrence be made less frequent and the percentage of 5 year "cures" increased. In an attempt to come to an understanding of the relative value of the wide removal of skin, the case records of patients subjected to radical mastectomy at The New York Hospital have been reviewed. In this analysis attention has been given to the relation of the use of a skin graft to the occurrence of local recurrence and to the rate of local recurrence as an indicator of the development of widespread metastases.

The basis of this study is the 255 patients on whom radical mastectomy was performed for carcinoma of the breast from September 1, 1932 to September 1, 1942. The shortest period of follow-up is 5 years. Operative surgery in these cases was done by 15 different surgeons, most of whom served as resident surgeon at the time. The basic steps of radical mastectomy followed the technique of Halsted: (1) preliminary biopsy with microscopic examination to ascertain the nature of the lesion; (2) preparation of the skin of the thigh as the donor site for a thick-split graft of skin; (3) use of a circular or elliptical incision about the tumor at a distance of at least 5 centimeters from its palpable margin; (4) extension of the incision from its central ellipse, superiorly to the middle or lateral third of the clavicle and inferiorly to the costal margin; (5) reflection of flaps of skin and a small amount of subcutaneous tissue superiorly to the clavicle, medially to the midsternum, inferiorly to a point below the costal margin, and laterally to the border of the latissimus dorsi muscle and the humeral insertion of the pectoralis major muscle; (6) detachment of the pectoralis major and minor muscles and their fasciae from their origins on the chest wall and their insertions into the humerus and coracoid process; (7) complete dissection of the axillary vein to permit removal of all of the contents of the axilla, including lymphatic vessels and glands, adipose and areolar tissue; (8) removal of breast, axillary contents, pectoralis major and minor muscles en masse; (9) reconstruction of a high axilla by obliteration of dead space and suture of the upper and outer cutaneous flap to the chest wall immediately posterior and inferior to the axillary vein; (10) suture of the margins of the cutaneous flaps superior to, medial to, and inferior to a central defect on the chest wall (suture is effected without undue tension while the arm is held in abduction at an angle of 90 degrees); (11) application of a thick-

From the Department of Surgery of The New York Hospital and Cornell University Medical College.

TABLE I.—ANALYSIS OF LOCAL RECURRENCE IN RELATION TO SIZE OF TUMOR, AXILLARY METASTASIS, AND THE USE OF A THICK-SPLIT GRAFT IN CLOSURE OF THE WOUND

With grafts

Diameter of palpable tumor centimeters	Axillary metastasis No.	Local recurrence No.	%	No axillary metastasis No.	Local recurrence No.	%	Total No.	Local recurrence No.	%
0–3	24	1	4	33	4	12	57	5	9
3–5	40	6	15	35	4	11	75	10	13
5–7	17	8	46	5	1	20	22	9	41
7+	26	12	46	8	4	50	34	16	48
Total	107(57%)	27	25	81(43%)	13	16	188	40	21

Without grafts

0–3	11	2	19	12	0	0	23	2	8
3–5	10	0	0	18	1	6	28	1	4
5–7	7	0	0	4	1	25	11	1	9
7+	4	0	0	1	0	0	5	0	0
Total	32(48%)	2	6	35(52%)	2	6	67	4	6

split graft to the residual open wound on the chest wall; and (12) application of a suitable dressing to maintain pressure upon the graft and the flap and to immobilize the arm in slight abduction.

Local recurrence of tumor developed in 44 (17 per cent) of the 255 patients. This was in general agreement with the reports of the surgeons who advocate the use of skin grafts in the closure of the wound of the chest wall and yet represented a higher percentage of recurrence than reported by surgeons who tend to avoid the use of skin grafts. Accordingly, the cases were divided into two groups on the basis of the use of a graft. This separation of cases showed that, contrary to expectation, the rate of local recurrence was considerably higher in patients in whom the wounds were closed with a graft than in those in whom closure of wounds was by primary suture of the margins of the flaps. There was local recurrence in 40 (21 per cent) of 188 cases in which a graft was employed. In 67 cases in which the wounds were closed without a graft there were recurrences in only 4 (6 per cent) (Table I). Because of the possibility that grafting had been used more frequently following the extirpation of large tumors and that this fact might account for the high rate of recurrence, attention was directed to the study of the size of the tumor in relation to the type of closure. Attention was also given to the presence or the absence of axillary metastases.

The patients were divided into four groups on the basis of the diameter of the primary lesion as measured before operation. Also the patients were divided into two groups on the basis of the presence and absence of axillary metastases. Since the surgeon is called upon to complete the radical mastectomy without accurate information as to the histopathology of the tumor and its relative malignancy, this study has concentrated on evaluation of the operative steps which are under control at the time of operation.

Review of the cases in which the tumor was small showed that grafts were used in closure of the wounds in 70 per cent of the cases. For the largest tumors, as one might expect, grafts were used in a higher percentage of cases; in this series 87 per cent. For the purpose of ascertaining the relationship of grafting to local recurrence, attention is devoted to the smaller tumors. Of the 154 cases in which wounds were closed with a graft, local recurrence developed in 24 instances (16 per cent). Of the 62 cases in which wounds were closed without a graft, local recurrence developed in only 4 (6 per cent) (Table II). In the group of patients with larger tumors local recurrence occurred in 16 of 34 patients whose wounds were closed with a graft, whereas no local recurrences developed in 5 patients whose wounds were closed without a graft (Table II). Thus the evidence on analysis of the small tumors foreshadows that of the large tumors. The use of grafting in the closure of the wound after a radical mastectomy has been performed is associated with a higher incidence of local recurrence.

In the development of local recurrence following radical mastectomy, the presence of axillary metastasis at the time of operation is a factor of importance. Of the 107 patients with axillary metastases and in whom the wounds were closed with grafts 27 (25 per cent) developed local recurrence. Of the 81 patients without axillary metastasis and with

TABLE II.—ANALYSIS OF USE OF THICK SPLIT GRAFTS IN RELATION TO SIZE OF TUMOR

Diameter of palpable tumor centimeters	With grafts No.	With grafts Per cent		Local recurrence No.	Local recurrence Per cent		Without grafts No.	Without grafts Per cent		Local recurrence No.	Local recurrence Per cent		Total cases No.
0—3	57	71	154	5	9	24 (16%)	23	29	62	2	9	4 (6%)	80
3—5	75	73		10	13		28	27		1	4		103
5—7	22	67		9	4		11	3		1	9		33
7+	34	87		16	48		5	13		0	0		39
Total	188	73		40	21		67	27		4	6		255

wounds closed with grafts, recurrence was noticed in only 13 (16 per cent) (Table I). The number of local recurrences in patients whose wounds were closed without a graft was too small to warrant conclusions. However, it is recorded that there were recurrences in 2 of 32 patients with axillary metastasis and recurrences in 2 of 35 patients without axillary metastasis (Table I).

Because of this evidence that axillary metastases predispose to a high percentage of local recurrence, it became necessary to cull from the available data the number of cases of axillary metastasis in which the wounds had been closed by skin grafts. Fifty-seven per cent of the 188 patients with grafts had axillary metastasis, whereas 48 per cent of the 67 patients without grafts had this complication (Table I). This difference is not great enough to parallel the comparative incidence of local recurrence in the two types of cases.

The size of the tumor at the time of operation had an important bearing on the incidence of local recurrence. This can be demonstrated in the patients with and without axillary metastasis. In the very small tumors, the rate of local recurrence was 4 per cent, whereas in the largest tumors, the rate of local recurrence approached 50 per cent (Table I).

The importance of local recurrence as a prognostic sign may be demonstrated by reference to Table III. Of the 255 cases studied, 125 patients (49 per cent) survived more than 5 years and in this group the rate of local recurrence was only 1.6 per cent. One hundred and thirty patients survived less than 5 years and in this group there were 42 local recurrences, a rate of 32 per cent. Seven local recurrences developed in 23 patients surviving less than 1 year (30 per cent), 24 in 72 patients surviving 1 to 3 years (33 per cent) and 11 in 35 patients surviving 3 to 5 years (31 per cent). Thus it may be stated that the development of local recurrence is almost positive assurance that death will occur within 5 years of operation. Thus local recurrence assumes an importance far beyond that of axillary metastasis, for 32 per cent of patients with axillary metastasis survived beyond 5 years, whereas only 1.6 per cent of patients with local recurrence did so. Although local recurrence is of grave prognostic significance, it is not at all clear whether local recurrence predisposes to or is merely a sign of general metastatic spread. Of the 44 local recurrences observed in the 255 cases under consideration, 17 appeared before any clinically evident spread had occurred elsewhere, 12 appeared simultaneously with and 15 after general spread. When local recurrence appeared following grafting (40 instances) it was as a nodule or two in the immediate vicinity of the grafted area in 27 cases (67.5 per cent), within the grafted area in 6 cases (15 per cent), and as innumerable foci on the chest wall in 7 cases (17.5 per cent).

DISCUSSION

The fact that local recurrence was found commonly in the skin of the chest wall about the grafted area suggests that surgeons had not been radical enough in the sacrifice of skin. The directions given by many surgeons for the performance of radical mastectomy include an

TABLE III.—ANALYSIS OF LENGTH OF SURVIVAL IN RELATION TO LOCAL RECURRENCE

Length of survival	Cases		Local recurrence	
	No.	Per cent	No.	Per cent
5 years or longer	125	49	2	1.6
Less than 5 years	130	51	42	32

admonition to space the elliptical or oval incision of the skin at a specified distance from the palpable margins of the tumor. The dictum that the local lesion should be skirted by at least 5, 7, or even 9 centimeters does not, it seems, give due importance to the fact that the larger the tumor the more likely has it spread a greater distance from its palpable margin. Thus, the suggestion is pertinent that the larger the tumor the more difficult it is to eradicate. Therefore, if wide skin excision be practiced for a small tumor, much wider excision must be practiced for the large tumor. Practice of this principle may make it possible to reduce the rate of local recurrence and to increase the percentage of 5 year survivals. That it probably never will be possible to avoid local recurrence entirely is shown by the fact that approximately 32.5 per cent of local recurrences appear within the grafted area, or as very widespread and innumerable foci. These foci may very well result from retrograde extension from residual intercostal and internal mammary lymphatics. It is on the 70 per cent of local recurrences which appear as discrete nodules near the grafted area or line of closure that the surgeon must concentrate. Obviously it is impossible to set down the specific spot at which the scalpel should be placed for each size of tumor. However, since the pectoral fascia, pectoral muscles, and axillary contents may be thoroughly excised, it would seem the logical next step to carry the proposals of Halsted, J. S. Rodman, Haagensen, Lewis and Rienhoff, and Eggers, de Cholnoky, and Jessup one step farther, and to excise proportionately more skin the larger the tumor rather than have a more or less fixed limit of cutaneous excision for tumors of variable size.

The only reason for failure to remove a very wide margin of skin is the surgeon's reluctance to have the patient left with a large defect on the chest wall. It is not new to call for wider removal of skin, for Lewis and Rienhoff found cause to state in 1932 that surgeons showed a tendency toward less radical excision of skin.

SUMMARY

The case records of 255 patients subjected to radical mastectomy for carcinoma of the breast have been made the basis of a clinical evaluation of the relation of skin grafting to local recurrence and the importance of local recurrence in the course of carcinoma of the breast.

Local recurrence developed in 44 (17 per cent) of the group of 255 patients. In 188 cases in which a graft was employed in closure of the wound, there were 40 instances of local recurrence (21 per cent), whereas in 67 cases of closure without a graft, there were only 4 instances of local recurrence (6 per cent). Approximately 70 per cent of the closures of wounds following radical mastectomy made use of grafts regardless of whether the tumor was less than 3 centimeters in diameter, 3 to 5 centimeters in diameter, or 5 to 7 centimeters in diameter. Following extirpation of tumors larger than 7 centimeters 87 per cent of wounds were closed with a skin graft. Axillary involvement was present with nearly equal frequency in those cases in which the wounds of mastectomy were closed with a graft (48 per cent) and in those closed without a graft (57 per cent).

The size of the tumor at the time of operation had an important bearing on the incidence of local recurrence. In tumors of the smallest size the rate of local recurrence was as low as 4 per cent, whereas in the tumors of largest size, the rate of recurrence was found to approach 50 per cent.

Local recurrence had an important bearing on the length of survival following radical mastectomy. In the 125 patients surviving more than 5 years, local recurrence developed in 1.6 per cent, whereas in the 130 patients surviving less than 5 years, the rate of recurrence was 32 per cent.

Of the 40 instances of local recurrence following grafting, 27 (67.5 per cent) appeared as solitary nodules in the immediate vicinity of the graft whereas only 13 (32.5 per cent) appeared within the grafted area or as multiple metastases both surrounding and within the grafted area. This situation gives rise to the thought that more radical excision of skin might give further protection against local recurrence.

Since the rate of local recurrence seems to be very closely related to the size of tumor at

the time of operation, it seems likely that local recurrence in the form of solitary nodules outside the area of grafting is related to insufficient removal of skin. The suggestion is therefore made that the excision of skin in radical mastectomy be more radical. With the improved methods of skin grafting now available, it seems indefensible that surgeons should not remove a truly wide area of skin at the time that radical mastectomy for carcinoma is carried out. The larger the tumor, the greater the need for very wide excision of skin.

REFERENCES

1. EGGERS, C., DE CHOLNOKY, T., JESSUP D.S.D. Ann. Surg., 1941, 113: 321.
2. HAAGENSEN, C. D. Surgery, 1946, 19: 100.
3. HAAGENSEN, C. D., and STOUL, A.P. Ann. Surg., 1942, 116: 801.
4. HALSTED, W. S. Ann. Surg., 1894, 20: 497.
5. Idem. Tr. Am. Surg. Ass., 1907, 25: 61.
6. HANDLEY, W. S. Cancer of the Breast and Its Operative Treatment. London: John Murray, 1922.
7. LEWIS, D., and RIENHOFF, W. F. Ann. Surg., 1932, 95: 336.
8. OLIVER, D. R., and SUGARBAKER, E. D. Surg. Gyn. Obst. 1947, 85: 360.
9. RODMAN, J. S. Ann. Surg., 1943, 118: 694.
10. STABINS, S. J. Surgery, 1946, 20: 684.
11. WHITE, W. C. Surgery, 1946, 19: 149.

THE OBSTRUCTED UTERINE CERVIX

GEORGE F. MELODY, M.D., San Francisco, California

NO pathological entity in the practice of obstetrics and gynecology is capable of more diverse manifestations than obstructive lesions of the uterine cervix. Such affections occur throughout the entire span of woman's life.

Complications of the obstructed cervix are encountered in practice from adolescence to senility. Some obstructions are congenital in origin, but the majority are acquired during postnatal life. Trauma, infection, neoplasms, radiation therapy, and senile atrophy are the leading etiologic factors. Despite their frequency, and the gravity of many of their sequelae, obstructions of the cervix, except for the excellent contributions of Curtis, have received but scant attention in the literature. It may be timely, therefore to review the general problem. Congenital malformations, pathological complications, prevention, and treatment are surveyed.

EMBRYOLOGICAL CONSIDERATIONS

Clinical experience would indicate that perhaps less than 10 per cent of obstructed cervices are congenital in origin. Developmental stenosis of the cervix may result from incomplete canalization of the distal extremities of the fused muellerian ducts. The obstruction in such cases may be situated at the external os ("pin-point os"), anywhere along the cervical canal, or at the level of the internal os. Curtis (8) has described the longitudinal ridges which traverse the length of the anterior and posterior cervical walls. From these elevations extend obliquely directed rugae, the *plicae palmatae*. The thickness of these ridges varies in different subjects, and it is known that hyperplasia sometimes occurs to such an extent that actual obstruction, particularly at the time of premenstrual congestion, takes place. Curtis cautions that without anesthesia at times it may be almost impossible to distinguish the resistance of the normal oblique folds from the resistance offered by the pathologically obstructed cervix; the obliquely directed rugae have the tendency to "catch" the uterine sound. Certain cervices may be stenotic at the external os only, the canal proper and internal os being patent. Stenoses at the internal os may be either apparent or real. In small anteflexed uteri it is often difficult to pass the standard uterine sound, whereas the No. 1 or No. 2 Hegar sound may be introduced with ease, especially if gentle traction is exerted by means of a tenaculum on the cervix, which tends to rectify the abnormal flexion in such uteri. In the study of a suspected stenosis, another useful technique is to bend the tip of the uterine sound at a much shorter and sharper angle, when it may be that the internal os may be passed without difficulty, whereas otherwise the tip of the sound may possibly impinge upon the posterior wall of the cervix.

In evaluation it may be said that although congenital strictures of the cervix may occasionally occur, their significance and precise pathogenesis remain a provocative subject for embryological, anatomical and clinical investigation. Examination under anesthesia is sometimes necessary to establish the presence of a genuine obstruction of developmental origin. The notion that most instances of primary dysmenorrhea are based upon a congenital stenosis of the cervix, is no longer tenable, although a small percentage of dysmenorrheic patients presenting a rigid, narrow cervix, particularly at the internal os, are benefited by dilatation of the cervix with or without the use of an intrauterine stem pessary (12, 27, 39).

ACQUIRED LESIONS

It is instructive to consider the wide variety of processes which have been found capable of producing an acquired stenosis or atresia of the cervix. A tabulation of the primary causes is presented in Table I.

From the Division of Gynecology and Obstetrics, University of California Medical School.

1. Infection. According to Ashton ulcerative changes in the vagina associated with diphtheria, scarlet fever, and smallpox, may close the external os. It is conceivable that intrauterine or neonatal infections of the lower genital tract may have the same effect. Gonococcal endocervicitis is a well known cause of cervical stricture. The lacerated and bruised puerperal cervix is fertile soil for bacterial invasion; fibrinous synechiae are readily converted into fibrous adhesions with subsequent stenosis. In certain instances of tuberculous endometritis enough specific granulation tissue may be elaborated in the region of the internal os, so that uterine drainage is obstructed and pyometra results. Cervical strictures are frequently associated with instances of chronic endocervicitis of undetermined etiology. The deposition of fibrous tissue in the cervix is always a probability in any cervix which has been the seat of an acute or chronic recurrent infectious process, regardless of the identity of the original infectious agent. Secondary bacterial invaders which are resident months or years after the original infection has been dealt with may have the ability to evoke more intense plastic reactive inflammation than has the primary infectious agent, whether gonococcal, streptococcal, or otherwise. In his chapter on soft tissue dystocia, Schumann cites syphilis among the processes being capable of producing a dense, undilatable stricture of the uterine cervix.

2. Trauma. Practically any instrumentation of the cervix may so traumatize the epithelium that cicatrization with resulting stenosis ensues. Sounding of the uterine cavity, which used to be a common office procedure, may lead to abrasion of the mucosa, scar tissue, and eventual stenosis. Dilatation and curettage if done too thoroughly can be traumatic; too vigorous curettage of the uterine cavity can lead to more or less complete ablation of functioning endometrium with subsequent permanent amenorrhea, as well as to removal of too much endocervical mucosa. Cauterization of the cervix, especially carbonization of the canal for endocervicitis, stands at the top of the etiologic list as the most frequent cause of cervical stenosis of traumatic origin. Kleegman warns of the hazard of cervical strictures and stenoses that attends electrosurgical methods of treating cervicitis. In the year 1906 Hunner recommended the Paquelin cautery in the treatment of chronic endocervicitis. In the year 1911 Dickinson used the fine wire nasal tip instrument for the treatment of cervicitis.

TABLE I.—ETIOLOGY OF THE OBSTRUCTED UTERINE CERVIX

- A. Congenital
  - Hyperplasia longitudinal cervical ridges
  - Incomplete canalization caudal ends muellerian ducts
- B. Acquired
  - Infection
    - Vaginitis
    - Cervicitis
    - Syphilis
  - Trauma
    - Pelvic delivery
    - Abortion
    - Instrumentation
    - Cauterization
    - Conization
    - Amputation
    - Trachelorrhaphy
    - Duehrssen's incisions
    - Hysterotomy, vaginal
    - Hysterectomy, supracervical
    - Caustic medicaments
    - Foreign bodies
  - Radium and x-ray
  - Neoplasms
    - Carcinoma cervix
    - Carcinoma corpus
    - Myomas
    - Adnexal tumors
    - Uterine calculus
  - Senile contracture

Shaw reports a fatal case of peritonitis resulting from cauterization of the cervix at the time of supracervical hysterectomy; autopsy traced the peritonitis to a postcauterization stump abscess. His comment is that the patient "might have been saved by more thorough dilatation of the cervical canal after cautery."

Amputation of the cervix, trachelorrhaphy and tracheloplasty have all been followed by stricture or stenosis of the remaining cervix. Block reports an incidence of cervical stricture in 9 per cent of the patients subjected to conization of the cervix. Hendriksen, in his report on 6,550 cervical stumps, calls attention to the occurrence of stricture in the "forgotten" stump, with occasional abscess formation in the cervical wall and cervical pyometra. The topical application of necrotizing chemicals, such as strong silver nitrate, chromic acid, and other corrosive substances, to

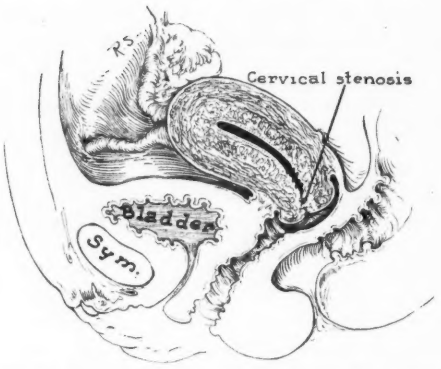


Fig. 1. The external os is the commonest site for stricture or atresia. This is the usual location for stenosis subsequent to cauterization of the cervix.

the cervical canal can evoke such tissue destruction that cicatrization and stenosis result. Frank relates how a forgotten piece of cervical gauze retained *in situ* for 2 years resulted in traumatic stenosis and hematometra. The perennial wearing of stem pessaries, whether for therapeutic or contraceptive purposes, may be followed by the same train of events. Israel and Harrel report 3 cases of severe pelvic inflammation which resulted from the employment of intracervical wishbone pessaries, used to achieve prolonged contraception. The indications and contraindications for stem pessaries have been thoroughly taken up by Weir, Douglass, and Melody.

Vaginal delivery, spontaneous or operative; abortion, spontaneous or induced; vaginal hysterotomy, Duehrssen's incisions of the cervix, and the repair of fresh puerperal lacerations of the cervix, all have been followed by stenosis and stricture in certain instances. Bernstein and Walter found that injury sustained during delivery, followed by infection, was the most common cause of cervical stenosis in a group of 8 patients who developed hematometra; such etiology accounted for 3 of their cases. Inept forceps rotations, with shearing of the endocervical mucosa, lay bare the field for the deposition of dense scar tissue and eventual stricture. Previous anterior vaginal hysterotomy has been seen to result in such a stenotic cervix that the next pregnancy required termination by cesarean section (30).

3. Radiation therapy. The fibroplasia and cicatrization subsequent to radiation therapy, whether radium or x-ray, is a well known cause of cervical stricture and stenosis. Arneson warns how the fibroplasia following x-ray therapy for cervical carcinoma may make virtually impossible the insertion of intrauterine radium at a later date. In the year 1929 Bland made an interesting report upon the occurrence of pyometra following radium therapy for uterine cancer. He regarded pyometra as analogous to pyonephrosis in the kidney, "where the dominant character is not the suppuration but the retention with distention of the organ." Carter analyzed 39 cases of pyometra from a bacteriological critique. He found that sterile pyometra occurred most frequently in uteri with carcinoma both before and after treatment, whereas no case of pyometra which occurred spontaneously, that is without previous operation or radiation therapy, was sterile. An interesting case of postradiation cicatrix of the cervix, with stenosis of the cervical canal and hematometra, occurring in a 35 year old secundipara who had previously received intrauterine radium for dysfunctional bleeding and subsequently estrogens to allay vasomotor symptoms of the menopause, has recently been reported (26). Estrogens activated the endometrium with resulting menstruation which was retained and gradually distended the uterus, drainage from which was obstructed, because of postradiation cicatrix of the cervix. When the uterus was opened following hysterectomy, the cervical canal was found to be completely obliterated, and the uterine cavity was full of blood, some fresh and some obviously old.

4. Neoplasms. Carcinoma of the uterine cervix, especially the endophytic variety, is a frequent cause of cervical obstruction with resulting pyometra. Corporeal carcinoma, if situated near the isthmus, may cause blockage of uterine drainage, with attendant pyometra. A cervical myoma which grows into the canal can so obstruct menstrual drainage that acquired dysmenorrhea and hematometra may result. A relatively small myoma situated in the lower uterine segment or cervix may so effectively block the birth canal that abdominal delivery is necessary. An impacted inter-

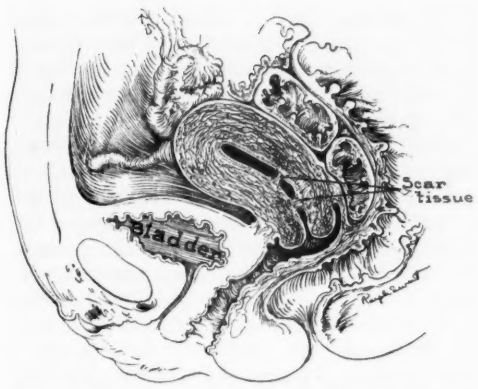


Fig. 2. Dense scar tissue is present at internal os and in the cervical canal. Such cicatrization has been encountered months or years after the use of intrauterine radium therapy.

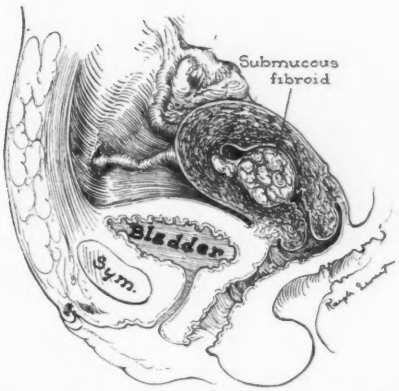


Fig. 3. Submucous myoma bulging into the uterine cavity, the caudal half of which is almost obliterated. Obstructed uterine drainage results from the ball valve action of such a myoma.

stitial myoma of the posterior cervical wall may be an absolute obstruction to vaginal delivery. A pedunculated submucous myoma, by protruding through the cervical canal in a ball-valve fashion, may give rise to severe reflex uterine contractions and effectively obstruct uterine drainage, until it has been "delivered" through the cervix. Carter quotes a report by Reeb in 1928, in which the latter recounts the case of a 77 year old woman with a calcified concretion, so called "womb-stone," blocking the cervix with the production of pyometra; the patient had undergone dilatation and curettage and radium application at the age of 44, for a small myoma. According to Scanzoni (32) obstructed uterine drainage may result from the extrinsic pressure of an ovarian cyst or neoplasm.

5. *Senile contracture.* Senile atresia or contracture of the cervix is a natural part of the process of postmenopausal involution of the genitalia. The cervix becomes smaller and more conical in appearance. If secretions from the endometrium accumulate and are trapped behind the cervix, bacteria, invading by way of the cervix, produce endometritis and eventual pyometra. This train of events may occur spontaneously in a cervix which has not been the seat of previous operation or malignancy. The syndrome of intermittent cervical obstruction in postmenopausal women, in which secretions accumulate, giving rise to backache and lower abdominal distress, only to be promptly relieved by the rather sudden escape of watery, blood-tinged leucorrhea, has been described by Faulkner. The indiscriminate use of estrogens in postmenopausal women who have a closed cervix often eventuates in activation of the endometrium with resulting bleeding, and trapping of the blood in the uterine cavity (hematometra). What with the ever-growing number of postmenopausal women, and particularly those who have had previous trauma, infection, or surgery upon the cervix, the production of hematometra from the injudicious use of estrogens is becoming more and more common.

SYMPTOMATOLOGY

A galaxy of syndromes may result from an obstructed uterine cervix, depending upon several variables, namely: (1) the location of the obstruction; (2) the degree of the obstruction, that is, whether complete (atresia) or incomplete (stenosis); (3) the manner in which the obstruction occurs, that is, whether congenital or acquired; (4) the period of the woman's life when the obstruction manifests itself, that is, the menarche, the childbearing, or the postmenopausal era; and (5) the nature of the trapped secretions, that is, inflammatory products or blood.

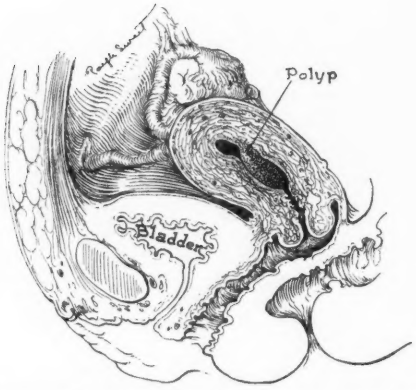


Fig. 4. Pedunculated fibroid polyp approaching internal os. Gradual growth of polyp results in its extrusion through the cervical canal.

1. Cryptomenorrhea. Obstructed uterine drainage may be manifested by delayed menarche. The patient often presents herself with a chief complaint of primary amenorrhea. Careful anamnesis, however, may reveal that the individual has had cyclic molimina, without, however, any external bleeding. The commonest site of obstruction in such instances is the external os. The retention of menstrual blood over a period of months or years may gradually distend the uterus so that it becomes a soft, symmetrically enlarged viscus the size of a gravid uterus of 3 or 4 months. The cervix may become converted into a smooth, soft mass at the apex of the vagina, the cervical canal having become ballooned out by the hematometra process. The external os may be hardly visible, and then only as a pigmented puckered point in the apex of the vaginal vault.

2. Dysmenorrhea. Curtis (9) states that "the pain of obstructed uterine drainage varies from ill-defined discomfort to severe cramps." It used to be widely held that the hypoplastic acutely anteflexed uterus, so often associated with primary dysmenorrhea, presented an actual obstruction at the internal os. However, many patients with such uteri complain of cramps hours or even days before there is the slightest suspicion of flow; hence the pathogenesis of pain in such cases is apparently based on some mechanism other than stenosis of the cervix. Very probably it is associated with hyperemic distention of the viscera. Weir (40) has found that bending the tip of the uterine sound at a much shorter and sharper angle will often permit it to pass the internal os, when otherwise the sound would obstruct against the posterior cervical wall at the level of the internal os. Traction on the cervix, by straightening the acute angle at the internal os, often helps in achieving passage. Nevertheless, in a rather small percentage of patients with a diminutive anteflexed uterus it will be found that the internal os is so narrow and rigid that even the small surgical sound can only be passed with the greatest difficulty. In such instances clots may form in the uterine cavity and require forceful "cramps" to expel them. Such a narrow, rigid internal os is almost certainly of congenital origin, and the dysmenorrhea might properly be called "obstructive."

An interstitial myoma in the cervix may gradually block the canal and give rise to severe acquired dysmenorrhea, from the reflex uterine contractions evoked in overcoming the obstruction. A pedunculated submucous myoma may give rise to continual uterine colic, until the tumor has been "delivered" through the external os.

3. Menorrhagia. Prolongation of the menses is frequently the presenting symptom in women of the childbearing age who have cervical obstructions. The period may last from 5 to 10 days, and the bloody discharge may be intermittent during the bleeding episode. Not infrequently the actual bleeding phase passes over into an interval during which there is a more or less persistent discharge of tarry material which may last practically until the onset of the next menses.

4. Leucorrhea. This is perhaps the commonest complaint caused by cervical stenosis in women in the reproductive and postmenopausal eras. Assuming that the usual infective incitants have been excluded, persistent or recurrent leucorrhea in women of the childbearing age will often be found to be associated with an obstructed cervix. As pointed out by Henriksen leucorrhea, odorless or malodorous, is a not uncommon complication of supracervical hysterectomy, and results from the de-

velopment of stricture in the remaining cervix. The obstruction is usually found at the external os, and, according to Henriksen, investigation will often disclose abscesses in the cervical wall or frank cervical pyometra. The tendency of the cervical stump to develop strictures has been attributed to impaired blood supply following ablation of the corpus uteri and to the cessation of the cyclic menstrual discharge through the cervical canal. The sudden onset of profuse leucorrhea in a postmenopausal woman requires that gynecologic investigation exclude the presence of cervical stricture. Gradual closure of the cervix is a natural concomitant of the genital atrophy seen in senile involution. Faulkner describes the syndrome of intermittent cervical obstruction in postmenopausal women, characterized by low backache, vague lower abdominal pain, and the sudden issue of a watery pinkish vaginal discharge. Dilatation and curettage done to exclude uterine malignancy reveals a stenotic cervix. The patient may remain asymptomatic for months or years, until secretions trapped behind the blocked cervix develop sufficient pressure-head to break through the obstruction, thus repeating the syndrome of intermittent cervical obstruction. The alternate retention and drainage of trapped uterine secretions after menopause has been known to go on for years. If bacteria invade the uterine cavity through the stenotic cervix, endometritis followed by pyometra ensues.

5. *Senile vaginitis.* If there is little or no response to the usual medical treatment for atrophic vaginitis, the possibility of cervical stricture should be investigated. Cicatricial changes in the postmenopausal cervix sufficient to block the lumen of the cervix are frequent. Bacterial invasion of the trapped secretions may produce copious inflammatory products which gradually build up pressure-head, and seep through the cervix. The thin, senile vaginal mucosa with its low glycogen content is readily irritated by such exudates. Without first establishing adequate surgical drainage of the retained inflammatory products, acidic vaginal douches and estrogens, which in the uncomplicated case of senile vaginitis are usually so salutary, are quite ineffectual.

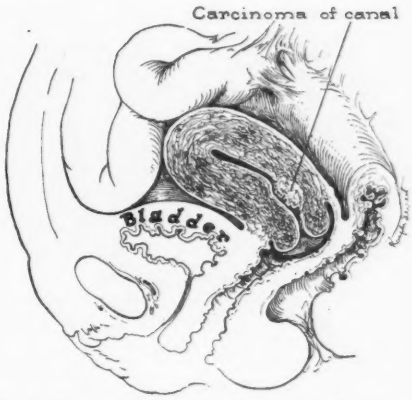


Fig. 5. Carcinoma of the cervix is one of the most common causes of pyometra.

6. *Postmenopausal bleeding.* In his analysis of 179 cases of postmenopausal bleeding TeLinde found 6 cases (3.4%) to be due to chronic endometritis. In 5 of the 6 cases pyometra was found at operation; in the sixth case no mention was made of it in the operative note. The cause of the pyometra in the 5 cases was a benign stenosis of the cervical canal associated with senile contracture of the cervix. The typical presenting complaint in these patients was a blood-tinged purulent discharge. Microscopic examination of the endometrium showed typical senile changes with the usual evidence of chronic inflammation. Pratt includes stenosis of the cervix among the many conditions which must be included in the differential diagnosis of bleeding associated with the menopause.

7. *Infertility.* Hamblen encountered cervical factors in 32 per cent of childless wives. Endocervicitis occurred in 22 per cent; poor drainage in 6 per cent; and, failure to receive spermatozoa in 4 per cent. Pin-point external os, or strictures of the canal, impede physiological drainage and lead to inspissation of the mucous plug, with resulting physical and chemical alterations in the cervical mucus which eventuate in impenetrability or chemical hostility to spermatozoa. Impaired drainage often leads to infection and *vice versa.* The finding of thick, opalescent pus in the external os during the mid-cycle, when the cervical secretion should normally be thin, transparent

and watery, is evidence of a pathological endocervix. In instances of cervical hostility microscopic study of semen aspirated from the cervical canal will show absence of motile sperm.

The first clue to an obstructed cervix may be the inability to pass the Jarcho cannula at the time of the proposed Rubin's test for tubal patency. The frequency of pregnancies following nothing more than tubal patency test, whether by gas or iodized oil, may well be due as much to the benefit of dilating the cervix, in passing the cannula, as to the actual perfusion of the testing medium through the uterotubal system.

8. Hematometra. This requires a complete obstruction of the lower genital tract and a functioning endometrium. Bernstein and Walter, in reporting 19 instances of hematometra, encountered 8 cases that resulted from cervical stenosis; the other 11 instances were congenital in origin, including imperforate hymen (10 cases) and bicornuate uterus (1 case). Trauma sustained during delivery, followed by infection (3 cases), was found to be the most common cause of stenosis. The other etiologic factors were cauterization, surgical removal of a cervical myoma, dilatation and curettage, x-ray and radium therapy, senile cervical contracture, and obstruction resulting from uterine myomas. Amenorrhea, lower abdominal pain, and a symmetrically enlarged soft uterine tumor are the typical findings in hematometra, as well as in pyometra. The formation of hematometra is much more spectacular and rapid in development in menstruating than in postmenopausal women. In menstruating women with cervical atresia the distended uterus may enlarge to the size of a 3 months' gestation in the matter of several months. Complaints referable to the abdomen may extend from a vague sensation of uneasiness to severe colic-like lower abdominal pain. Hematometra as a sequela to the obstructed cervix is being encountered more frequently nowadays, as a result of the universal use of cervical cauterization, the frequent utilization of conization of the cervix, and the not infrequent employment of radiation therapy. The case records of the Massachusetts General Hospital have recently included 3 most interesting instances of hematometra, resulting from the administration of estrogens to relieve menopausal symptoms in women with obstructed cervices. The first patient (23) was a 54 year old woman who developed cervical stenosis as a result of conization of the cervix 4 months previously. The second instance (26) was a 35 year old secundipara whose cervical obstruction resulted from the administration of radiation therapy (radium) 8 months previously for the control of dysfunctional uterine bleeding. A common complication of estrogenic therapy is the so called withdrawal bleeding; a frequent sequela of operative procedures to the cervix is stenosis or atresia, resulting from cicatrization.

9. Hematosalpinx. Retained blood may proceed reflux to distend the fallopian tubes (hematosalpinx). If the fimbriated end of the tube is closed pyohematosalpinx may develop. The clinical picture of pyohematosalpinx is indistinguishable from acute salpingitis. If the fallopian tubes are open, blood forced into the tubes from the uterus, may escape into the peritoneal cavity, and there produce varying amounts of hematoperitoneum. Although tubal pregnancy is the most common cause of hematosalpinx, it is well to remember that the latter may be a complication of gynatresia. The fimbriated end of the tube may close as a result of infection, as in salpingitis, or of aseptic inflammation, as in tubal pregnancy.

10. Pyometra. The distention of the uterine cavity with inflammatory products gives rise to much the same symptomatology as is encountered in hematometra. In addition to the lower abdominal discomfort, there may be chills and fever, and other evidence of sepsis. The serosanguineous material associated with the pus is thought to be the result of bleeding from the granulation tissue lining the pyogenic membrane into which the uterine cavity is converted. Occasionally the pyometra may result in such a rapid enlargement of the uterus in a postmenopausal woman that cellular myoma or sarcoma may be misdiagnosed and lead to needless hysterectomy (14). An unsuspected pyometra may be revealed in the routine investigation of abnormal uterine bleeding resulting from carcinoma of the cervix, an extremely common cause of pyometra.

11. Endometriosis. The pathogenesis of endometriosis has not been established; however, it seems not unlikely that an occasional case, at least, may result from reflux menstruation, according to Sampson's theory. In patients suspected of having pelvic endometriosis finding the uterus in normal upright position should invite investigation of the cervical canal as to patency. Curtis (8) has found that a not uncommon cause of obstructed drainage is hyperplasia of the longitudinal ridges of the cervix.

Fullerton (17) feels that reflux menstrual discharge is the etiological factor in perhaps the majority of cases of endometriosis. He believes that a tight cervix can be the cause of reflux pertubal menstruation. Maintaining that at the time of dilatation of the cervix with the usual solid metal dilators the intrauterine pressure is increased by the piston-like action of the dilators, Fullerton has suggested that the ordinary dilators be modified by boring a tubular lumen (1 mm. in diameter) longitudinally through the center, thus eliminating the piston action within the uterine cavity, which he calls an anatomic syringe barrel.

12. Conglutination of the external os. In this rather unusual obstetrical complication the presenting part is well engaged in the pelvis, the cervix thin and effaced, and tightly stretched over the presenting part, but the os fails to dilate beyond a pin-point opening, the margins of which are rigid and sharp. This condition is more common in primiparas than in multiparas, but has been known to recur in succeeding pregnancies (36). The stenotic external os usually very promptly opens in response to digital insinuation; rarely, Duehrssen's multiple incisions are required.

13. Cervical dystocia. It is recognized that cervical dystocia may result from a galaxy of obstetrical conditions, including neurogenic inhibition, uterine inertia, and cephalopelvic disproportion; however, previous surgical or other trauma to the cervix may evoke such cicatrization that the cervix will fail to efface and dilate during labor. Failure to recognize such a complication may result in rupture of the uterus (4). The correct treatment is cesarean section, after a reasonable and closely supervised trial of labor. Certain instances of rupture of the uterus of rather obscure etiology may be traced to the sudden giving way of a badly scarred cervix, with extension of the rupture into the broad ligament (18).

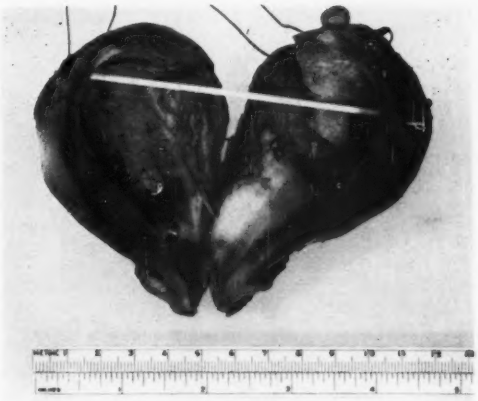


Fig. 6. Specimen removed from a 36 year old nulligravida. Complaints included primary dysmenorrhea, sterility, and menometrorrhagia. The small surgical probe could not be passed through the cervical canal. The cavity was greatly distended from hematometra, and the uterine wall was one-third normal in thickness. The rather large submucous myoma situated in the fundus uteri was an incidental finding. Note the dense scar tissue in the cervix and the lower uterine segment. The cause of the extensive cicatrization could not be ascertained. (Specimen, courtesy of Dr. John A. Driscoll.)

14. Postpartum pyometra. Reycraft (31) has pointed out the importance of stenosis of the cervix with retention of lochia and pyometra as a cause of puerperal morbidity. The usual history is an operative vaginal delivery, followed a week or two later by chills and fever, a tender distended uterus, and scant or absent lochia. The same clinical picture may be seen following cesarean section, especially when the section has been done for cervical dystocia after a test of labor. Recovery is usually quite prompt, after the establishment of adequate surgical drainage by T-tube catheter, introduced after gentle dilatation of the closed cervix.

TREATMENT

Historical notes. Sir James Young Simpson (1811–1870) (33) quotes the Hippocratic writings (13th section) wherein the writer recommends that if the cervical orifice be very much contracted, it be opened by means of bougies

Fig. 7. Photomicrograph showing chronic endometritis, associated with pyometra in postmenopausal woman with benign contracture of the cervix. Uterus globular shaped, rapidly grew to size of 4 months' pregnancy. Hysterectomy was done because of suspicion of malignant myoma. There is extensive, diffuse infiltration of the endometrium by lymphocytes and plasma cells. Note two large foreign body giant cells; frequently encountered in any pyogenic membrane. (Specimen, courtesy Dr. Robert L. Faulkner.)

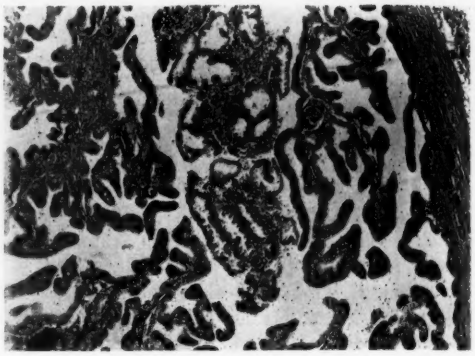


Fig. 8. Photomicrograph of transsection through normal uterine tube at time of menstruation. Note islands of menstruating endometrium free in tubal lumen. Reflux menstruation may be of etiologic importance in some instance of endometriosis. Cervical obstruction, uterine retrodisplacement, and increasing intrauterine pressure by the use of solid cervical dilators may be factors in promoting retrograde menstruation. (Specimen, courtesy of Dr. Robert L. Faulkner.)

and leaden instruments. Simpson also refers to a textbook entitled *Marrow of Chirurgery* by one Mr. Cook, a practitioner of Warwick, in which the author, in speaking of "closure of the 'inner orifice' of the womb, or os uteri, recommends it to be enlarged when necessary by gentian root or prepared sponge, and afterwards by the introduction of hollow instruments of silver, ivory or horn, and these means, he adds, are better than incision." Simpson himself advocates surgical division of the cervix, along its entire length, with an instrument he called the "hysterotome or metrotome." Scanzoni (32) describes his method of evacuating retained menstrual blood in cases of hematometra, by means of introducing a trochar into the most "depending and accessible point of the tumor which the lower portion of the womb forms in the vagina." He reports having treated 3 such cases of congenital obstruction at the external os with associated hematometra by the aforementioned approach without a fatality, and without complications.

1. Dilatation of the cervix. Opening of the obstructed cervix by means of dilating instruments is the most commonly done surgical procedure in the management of stricture. When difficulty is encountered in introducing graduated dilators, such as those of the Hegar type, much can often be accomplished by employing a spreading or divulsing instrument, such as the Atlee dilator. The latter will often be successful in reopening the natural passageway, when a tubular dilator will make no advance whatsoever. If graduated dilators are used, it is essential to have available the smallest ones, including the Hegar No. 1 and No. 2, which are usually not included in the ordinary set-up for dilatation and curettage. Web-like curtains at the external os can often be opened with the smaller surgical probes, if only the puckered point indicating the obliterated external os can be identified. Caution and gentleness should be the watchword in approaching these cases, particularly if there be an associated pyometra or hematometra.

2. Dilatation of the cervix and stem pessary. In the occasional stricture, without any associated infection, including cervicitis and adnexitis, the intrauterine silver stem of the Chambers type may be used to advantage, after the obstruction has been overcome. The stem may be left in place for 3 to 6 months, to insure maintenance of established patency.

As recommended by Weir and Melody a vaginal pessary of the Smith or the Hodge type should be worn concomitantly with the stem, to prevent expulsion of the latter. Potter recommends a winged stem pessary to correct stenosis of the external os in certain selected cases of involuntary sterility. He reports having used such a device in 12 patients, in 8 of whom pregnancy subsequently occurred. In Potter's series sterility investigation was entirely negative except for stenotic cervix with associated cervical hostility, as demonstrated by the Huhner postcoital test.

3. Dilatation and evacuation. This is the procedure of choice in instances of pyometra and hematometra. Adequate surgical drainage of the trapped uterine contents may be insured by inserting a rubber T-tube catheter, such as is used in draining the common bile duct; the catheter should remain until drainage has been complete, which may be a matter of several days to several weeks. This is the ideal procedure for puerperal pyometra. Bacteriological cultures should be taken and processed anaerobically and aerobically.

4. Anterior lip bisection. Very rarely, if the obstruction cannot be opened by divulsion (Atlee and Goodell dilators) or by dilatation (surgical probes and small Hegar dilators), it may become necessary to advance the bladder and to make a small incision in order to find the strictured canal. This approach has been advocated by Curtis (10). Patency may be maintained by means of an intrauterine stem pessary or small rubber T-tube catheter, the choice depending upon the presence or absence of infection and trapped secretions.

5. Vaginal myomectomy. Certain obstructing cervical myomas can best be enucleated by the vaginal approach, after advancing the bladder. Pedunculated submucous myomas are best removed by snare or by ligation and division of the pedicle, if the latter be accessible; otherwise, morcellation may be the procedure of choice. Caution must be taken in dividing the pedicle lest the fundus uteri may be cut across, inasmuch as the fundus in such cases is sometimes inverted by the traction exerted by the pedunculated tumor. The transperitoneal removal of a pedunculated submucous myoma at the time of abdominal hysterectomy is mentioned to be condemned, because of the grave risk of peritonitis from contaminating the peritoneal cavity.

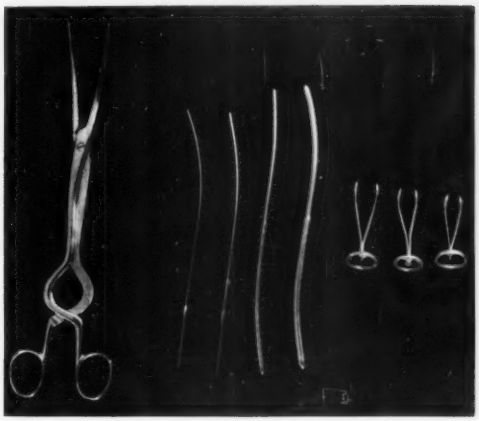


Fig. 9. Instruments for opening strictured cervix. On the left is the Atlee cervical dilator. In the center are Hegar dilators, sizes 1, 2, 3/4, 5/6 French. These smaller sizes are usually not included in the routine setup for dilatation and curettage. On the right are intrauterine silver stem pessaries which may be used in selected cases for maintaining patency.

6. Hysterectomy. Vaginal or abdominal hysterectomy may be the procedure of choice in certain instances of symptomatic stricture of the cervix, particularly in women over the age of forty. This may be especially indicated if there are such complaints as increasingly severe dysmenorrhea and persistent vaginal discharge, and if the uterus is enlarged and tender to palpation. Greenhill prefers vaginal hysterectomy in such cases.

7. Radiation. When uterine cancer is associated with pyometra from impaired uterine drainage, intrauterine radium is to be avoided until all evidence of infection has disappeared, if metritis, pelvic cellulitis, and peritonitis are to be averted. Preliminary x-ray is in order after surgical drainage has been established; the sterilizing effect of roentgen rays in such situations is most striking.

8. Cesarean section. The rationale of timely abdominal delivery in genuine cervical dystocia is obvious, if obstructed labor and possible uterine rupture are to be avoided.

9. Antibiotics. Depending upon the bacteriological findings either penicillin or strepto-

mycin may be indicated in the prophylaxis of complications after evacuating a hematometra or pyometra. Antibiotics are to be regarded as an adjunct, not a substitute for, surgical drainage.

PREVENTION

The guiding principle with regard to the therapeusis of the cervix uteri should be *primum non nocere*. Accouchement forcé and delivery through the incompletely dilated cervix have no place in modern obstetric practice. It is noteworthy that in a recent analysis of 77 cases of "failed forceps" in patients admitted to three Dublin hospitals for treatment, the cervix was not fully dilated in half of the patients (15). Great care and due gentleness must be observed whenever forceps rotations are required, lest damage to the cervix, with subsequent cicatrization, be sustained. Fresh cervical lacerations and Duehrssen's incisions must be repaired meticulously. Patients who have been subjected to such operative procedures should not be discharged 6 weeks postpartum; instead, they should be rechecked 3 or 6 months later, for possible cervical stricture or atresia.

The widespread use of cauterization, conization, cervical repair and amputation, intrauterine radium and pelvic irradiation have taken their toll in cicatrized cervices. It is recognized that the persistent administration of estrogens for the menopausal syndrome not infrequently activates a dormant endometrium into bleeding. If the cervix is closed hematometra may follow; this train of events is becoming more and more frequently observed. In passing it might be stated that the use of estrogens in not a few instances has been indeed casual. Patients who have been subjected to operative procedures on the cervix, including supracervical hysterectomy, or radiation therapy, should be followed at regular intervals, on which visits the cervix should be inspected, palpated, and sounded (with all due aseptic precautions) to ascertain and maintain patency of the canal. The Atlee cervical dilator is ideal for this purpose, although the smaller Hegar instruments may be quite satisfactory. If a high-grade stenosis is encountered, dilatation may have to be carried out under anesthesia. Cauterization and conization demand periodic follow-up observations for at least 6 months.

SUMMARY

The general subject of the obstructed uterine cervix has been reviewed. The natural history of cervical obstructions, as well as the clinical syndromes associated therewith, has been considered. A plea has been made for the avoidance of trauma to the cervix, both in obstetric and gynecologic practice. A critique of the various methods available in the management of the obstructed cervix has been presented. It has been emphasized that obstructive lesions of the uterine cervix are far from a rarity in everyday practice, and will be encountered with increasing frequency as the clinician becomes mindful of their possibility in his evaluation of obstetrical and gynecological problems.

REFERENCES

1. Arneson, A. N. Progress in Gynecology. Edited by Meigs, J. V., and Sturgis, S. H. P. 366. New York: Grune and Stratton, 1946.
2. Ashton, W. E. Practice of Gynecology. 2nd ed., p. 473. Philadelphia: W. B. Saunders Co., 1906.
3. Bernstein, P., and Walter, R. Am. J. Obst., 1939, 37: 126–136.
4. Bill, A. H., Barney, W. R., and Melody, G. F. Am. J. Obst., 1944, 47: 712–717.
5. Bland, P. B. Am. J. Obst., 1929, 17: 528–536.
6. Block, F. B. Am. J. M. Sc., 1943, 206: 794.
7. Carter, B. Am. J. Obst., 1942, 44: 1074–1090.
8. Curtis, A. H. Textbook of Gynecology. P. 30. Philadelphia: W. B. Saunders Co., 1947.
9. Ibid., p. 503.
10. Ibid., p. 626.
11. Dickinson, R. L. Am. J. Obst., 1921, 2: 600.
12. Douglass, M. Ohio M. J., 1944, 40: 821–823.
13. Faulkner, R. L. Unpublished data.
14. Idem. Personal communication.
15. Feeney, J. K. Irish J. M. Sc., 1947, 257: 190–210.
16. Frank, R. T. Obstetrical and Gynecological Pathology. P. 179. New York: D. Appleton & Co., 1922.
17. Fullerton, W. D. Am. J. Obst., 1932, 24: 142–143.
18. Gordon, C. A., and Rosenthal, A. H. Surg. Gyn. Obst., 1943, 77: 26–30.
19. Greenhill, J. P. Year Book of Obstetrics and Gynecology. Pp. 394–395. Chicago: The Year Book Publishers, 1942.
20. Hamblen, E. C. Endocrinology of Woman. P. 494. Springfield: Charles C Thomas, 1945.
21. Henriksen, E. Am. J. Obst., 1939, 37: 452–457.
22. Hunner, G. L. J. Am. M. Ass., 1906, 46: 191.
23. Ingersoll, F. M., Castleman, B., and Ulfelder, H. N. England J. M., 1947, 237: 525–526.
24. Israel, S. L., and Harrel, D. G. Am. J. Obst., 1947, 53: 684–687.
25. Kleegman, S. J. Am. J. Surg., 1940, 48: 294–310.
26. Meigs, J. V., and Mallory, T. B. N. England J. M., 1947, 237: 746–747.

27. MELODY, G. F. West. J. Surg., 1947, 55: 544–549.
28. POTTER, J. C. Am. J. Obst., 1946, 52: 164–165.
29. PRATT, J. P. J. Am. M. Ass., 1947, 135: 562–564.
30. REYCRAFT, J. L. Personal communication.
31. Idem. Unpublished data.
32. SCANZONI, F. W. VON. Practical Treatise on Gynecology. Pp. 208–215. New York: Robert De Will, 1861.
33. Ibid., pp. 90–91.
34. SCHUMANN, E. A. Textbook of Obstetrics. P. 564. Philadelphia: W. B. Saunders Co., 1936.
35. SHAW, H. N., and GASPAR, J. West. J. Surg., 1947, 55: 81–86.
36. SIMPSON, J. Y. Clinical Lectures on Diseases of Woman. Pp. 101–119. Philadelphia: Blanchard and Lea, 1863.
37. TELINDE, R. W. South. M. J., 1930, 23: 571–576.
38. TITUS, PAUL. Management of Obstetrical Difficulties. 3rd ed., p. 457. St. Louis: C. V. Mosby Co., 1945.
39. WEIR, W. H. Am. J. Obst., 1937, 33: 291–297.
40. Idem. Personal communication.

THE TECHNIQUE OF SURGICAL DIVISION OF PATENT DUCTUS ARTERIOSUS

OWEN H. WANGENSTEEN, M.D., F.A.C.S., RICHARD L. VARCO, M.D., and IVAN D. BARONOFSKY, M.D., Minneapolis, Minnesota

WHEN Robert Gross (6) successfully interrupted the continuity of the ductus arteriosus he released an attack, renewed in many surgical clinics, upon crippling congenital vascular lesions which has brought laurels to surgery and help to patients whose condition heretofore was believed unremediable. Anomalies of embryological development which aroused only occasionally the curiosity of students of pathology now have become the absorbing interest of many surgical clinics as well as the subject of everyday table-talk and newspaper comment. Such is the power of a ferment! Blalock's (1) bold and well conceived rehabilitation of the cyanotic child with pulmonic stenosis from invalidism to limited activity has caught the public imagination as few things in medicine ever have. And Crafoord's courageous excision of the strictured area in coarctation of the aorta has won the admiration of all physicians.[1] These technical accomplishments of surgeons have lent exciting interest to the correction of crippling congenital vascular anomalies—and hope to many, born to bear the tragic burden of an imperfection in a vital area.

When the history of surgery of this era is written, the importance of the stimulus to vascular surgery of Gross's successful interruption of the patent ductus will be generally appreciated. Gross has told the story of previous unsuccessful attempts at ligature of the ductus and how he worked out the details of the operative approach upon the dog. It perhaps is not without interest to relate here that Dr. George E. Fahr, Professor of Medicine, suggested to one of us in 1935 that he considered ligature of the patent ductus a feasible and desirable surgical venture. When the late Elliott Cutler came out from Boston in February, 1935, to give the E. Starr Judd Lecture in surgery at the University of Minnesota Medical School, Doctor Fahr showed us a 22 year old patient with a large heart and signs of impending cardiac failure from a patent ductus. Cutler, an experienced investigator in cardiac surgery, suggested that a Parham band be placed around the ductus if the operation was undertaken. Probably, fortunately for the patient, she declined an operation which had not yet then been performed. The first patient selected by Gross for the operation was a child of 7 years. All who have had an experience with the procedure of ligature or division of the ductus can well understand the difference in the surgical problem posed by a child of 7 and a large woman of 22 years with a large heart.

LIGATURE OR DIVISION?

Dissatisfaction with simple ligature of the ductus owing to the circumstance that recanalization occurred now and then persuaded Gross (7) to divide the ductus. This suggestion has been taken up in this clinic too, and for the same reason. Dr. M. J. Shapiro, who stimulated local interest in this problem following the initial report of Gross and who was responsible for the selection of all the patients for operation in the early stages of the effort here, estimates that recanalization occurs in approximately 10 per cent of patients after ligature. Our own experience in this clinic during the period when ligation was done (September, 1939 to November, 1941) is in accord

From the Department of Surgery, University of Minnesota, Minneapolis, Minnesota.

This work was supported by the Searle Fund for Surgical Research and a grant from the Graduate School of the University of Minnesota.

[1]Publications on the surgery of coarctation of the aorta by Gross and Crafoord appeared almost simultaneously. The paper of Gross and Hufner appeared in the *New England Journal of Medicine* for September 6, 1945, volume 233, page 257; that of Crafoord and Nylin in October *Journal of Thoracic Surgery* 1945, volume 37, page 347. Gross's first patient was operated upon June 28, 1945, Crafoord's on October 19, 1944. Crafoord's publication carries the following editorial footnote: "Received for publication June 1, 1945."

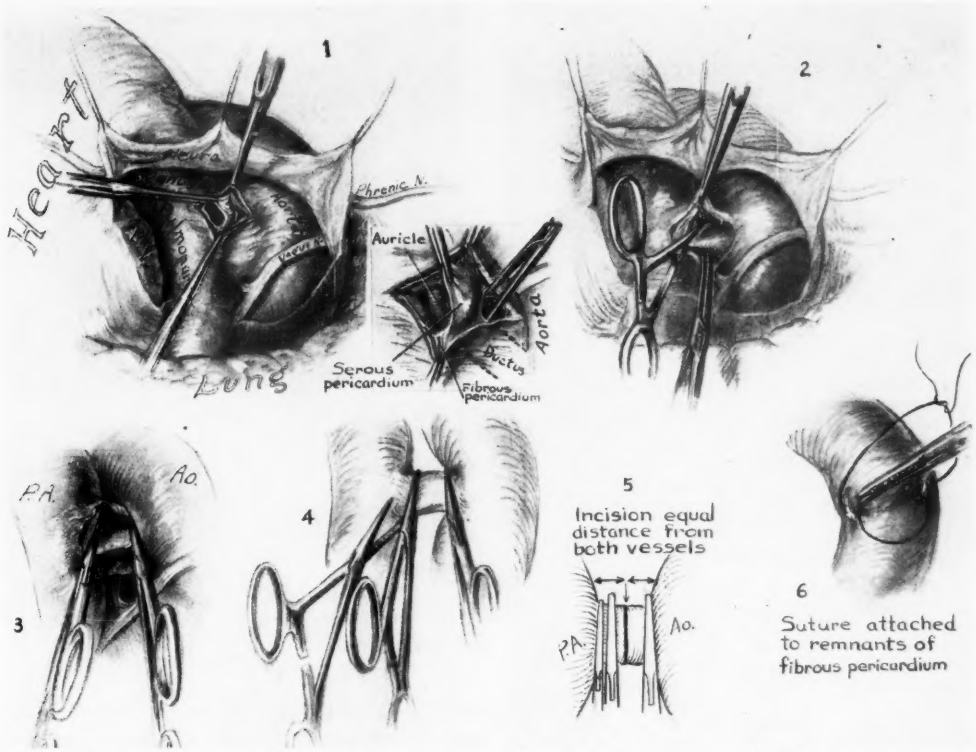


Fig. 1. Surgical division of the ductus. *1*, The exposure after division of the mediastinal pleura behind the phrenic nerve. The dissection of the fibrous pericardium overlying the anteromedial angle between pulmonary artery and aorta is commenced. *2*, A curved hemostat is pushed through from the outer side of the ductus after a communication has been established between the inner and the outer dissection. The illuminated lucite dissector shown in Figure 2 is a helpful agent in indicating the direction of the dissection in the inner medial angle between pulmonary artery, ductus, and aorta as well as in the final stages of the dissection. The separation of the thick fibrous layer of the pericardium from the thin inner serous layer is shown in the insert between *1* and *2*. *3* and *4*, Application of hemostats after completion of the dissection. The long hemostat shown in Figure 3a facilitate the operative procedure. *5*, The ductus is divided with a knife. Three or four hemostats or clamps may be applied; if only three are employed, a longer cuff is left on the aortic side as is shown in the diagram. Freeing the fibrous tissue from the adjacent vessel wall enlarges the working distance between ductus, pulmonary artery, and aorta such that the hemostats may be placed more readily upon the ductus (see text). *6*, The upper clamp has been removed and a running suture of fine silk (No. 0000 or No. 00000) is employed to oversew the cuff. A No. 000 silk suture is anchored in a remnant of the fibrous pericardium just beyond the site at which the clamp grips the vessel wall; that site should be as near the vessel wall as possible, certainly less than 2 millimeters from the grasp of the vessel wall in the clamp. The accurate placement and ligature of this suture insures complete hemostasis.

with such a suggestion. Among 16 patients in which simple ligature of the ductus was done, recanalization occurred in 2 patients.

There is by no means, however, complete unanimity amongst surgeons that division is preferable to ligation. The discussion (9) following a recent paper by Gross (8) in 1947 indicates clearly that some surgeons dissent from the opinion that division of the ductus is a better operation. Even so experienced and accomplished a thoracic vascular surgeon as Blalock (2) in 1946 appears to favor ligature over division of the ductus. The basis of this difference in attitudes is the circumstance that mere ligature is a simpler and safer operation than division; otherwise, everyone would agree that division is the safer operation from the standpoint of avoidance of recanalization.

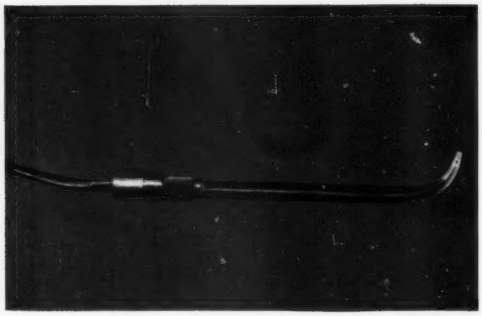


Fig. 2. The illuminated lucite dissector employed to indicate the direction of the dissection as well as the final establishment of a communication between the inner and outer dissection. It is attached to a low voltage battery commonly employed for operating room cauteries. During its use the area in which the penetration is to be accomplished may be more readily observed by cutting off temporarily all other sources of illumination.

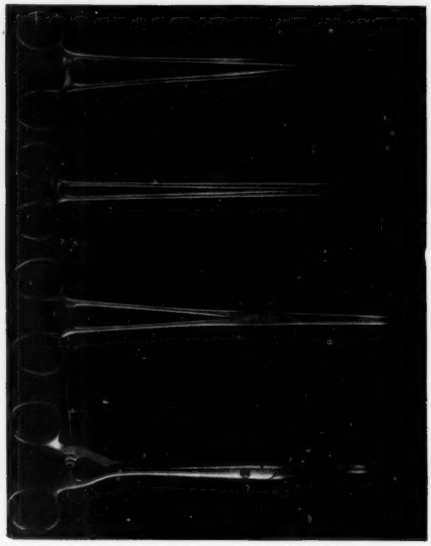


Fig. 3. Other special instruments employed in the dissection. a, A long narrow straight hemostat. b, A long needle holder. c, A curved dissector. d, An ordinary curved clamp (Guyon-Pean) for grasping the kidney pedicle is employed to complete the dissection shown in Figure 1, 2.

Certainly, no one would approve of simple ligature of an arteriovenous communication in an extremity. The difficulties and hazards of reoperation for patent ductus are even more real than for a peripherally located arteriovenous fistula. Why not take maximal pains therefore to thwart the possibility of recurrence in the first operation?

SURGICAL DIVISION OF THE DUCTUS

In 1944, and again more recently in 1947 Gross (7, 8) has outlined the plan of operation for division of the ductus. Since the publication of his first paper upon the technique, we have followed his general plan of operation with minor variations. An anterior incision is employed, usually obliquely across the anterior chest wall, occasionally beneath the breast, when it is well developed. The problem of the dissection is not a simple matter, particularly in older patients in whom both the heart and the pulmonary artery may be large. Moreover, the ductus itself, as well as the walls of the adjacent pulmonary artery and aorta, is not as tough as the fibrous layer of the pericardium from which it must be separated. This circumstance affords a real handicap in any dissection. And when the tissues to be separated are deeply situated and are conduits for blood, the difficulties are apparent. As Gross has indicated, when a lappet of pericardium covers the ductus anteriorly only, it may be dissected off. More often than not, however, in our experience the medial wall of the ductus, in the plane which must be developed in the dissection between the aorta and the pulmonary artery, appears to be well supported by a reflection of the pericardium. Earlier in our experience, and especially in adults with large hearts, when the dissection in the anteromedial angle between aorta and pulmonary artery seemed difficult, we resorted to the expedient of deliberately opening the pericardial sac over the root of the pulmonary artery, separating the outer fibrous from the inner thinner serous layer of the pericardium. This separation facilitates the dissection. With increasing experience, however, the necessity for opening the pericardial sac to identify the outer fibrous layer of the pericardium has become very infrequent. Removal of the fibrous layer of the pericardium from the ductus without injury to its wall is essentially the problem posed by the operation. With the fibrous layer of the pericardium removed from the ductus, progress in the dissection is readily

discerned. Whereas, some separation is permissible by employment of a blunt curved hemostat, it is our plan in the main to perform the entire dissection under direct vision, using scissors and elevating tissues to be dissected off the wall of the ductus with hemostats. A curved, illuminated lucite elevator or dissector has been very helpful in identifying the plane through which the dissection should proceed. By grasping with a hemostat the areolar tissue (probably remnants of the serous layer of the pericardium), lying directly over the top of the illuminated lucite elevator, an opening is made, establishing a direct connection between the medial and the lateral portions of the dissection. One of us (O. H. W.), who is partial to this maneuver in completing the dissection, employes this technique routinely, frequently switching off all other operating room lights to facilitate identifying and dividing the areolar tissue, at the innermost posterior angle, tipped forward by the illuminated lucite dissector, which has been pushed beneath the ductus from its lateral aspect. Once penetration through the fibrous pericardium surrounding the ductus is achieved, enlargement of that orifice is readily accomplished by elevating and cutting the edges of the adjacent fibrous tissue.

Inasmuch as the wound is often deep, long straight narrow hemostats of the Halsted or Rankin pattern have been made up to facilitate division of the ductus (Fig. 3a). Four such clamps are placed; care also is observed to avoid the recurrent laryngeal nerve with placement of the uppermost clamp on the aortic side and each clamp is pushed home to the last notch on the clamp. The ductus is cut with a knife between the two middle clamps. In the placement of the clamps, it is important to have the tip of the clamp just grasp the inner wall of the ductus. Following division, a No. ooo silk suture is placed at the inner angle in the remnants of the fibrous pericardium, immediately adjacent to the ductus wall at the level of the lower clamp, before the upper one is removed. This suture is simply a safety device rarely needed but very convenient to permit elevation of the inner angle should there be any difficulty with subsequent steps in the operative technique. Such a suture is placed on both the pulmonary artery side as well as the aortic side of the ductus before the upper clamp on each side is removed. The illuminated lucite dissector, mentioned previously, is an extremely useful instrument too in deciding that the lower clamp on each side actually has the entire vessel wall in its grasp. Should the surgeon have any misgivings on this score the placement of a mattress suture of fine silk (No. oooo) at the inner angle between the upper and lower clamps, before the latter is removed, will eliminate any potential hazard ensuing from failure to place the lower clamp completely across the arterial wall. Strange as it may seem, it is occasionally difficult to decide definitely exactly where the vessel wall ends and where the periarterial fibrous tissue begins. Following the example of Gross, we place a running suture of fine silk (No. oooo or No. ooooo) over the remnant or cuff of tissue projecting above the lower clamp. However, before removing the remaining clamp, an additional stick-tie or horseshoe suture of No. ooo silk is anchored with great care in the remnants of the fibrous pericardium, immediately adjacent to the duct wall. As the remaining clamp is removed, this ligature is tightened and tied so that complete hemostasis is insured. The exact placement of this suture requires the greatest care, for it is an important item in the safety of division and ligation of the ductus. In the manipulation of the clamps following division of the ductus, everyone touching a clamp is cautioned to hold it only by one shank or ring, thus precluding any inadvertent releasing action occasioned by manipulation of both handles of the clamp.

RESULTS

Every patient whose patent ductus arteriosus has been interrupted by us since this series of operations began, following Gross's publication on division of the ductus has had operative division of the ductus employing the principles of the technique described herein. On several occasions, confronted with a wide, but short and deeply located ductus in a large subject, it has been difficult to resist the temptation of simply ligating the ductus. It is in just such cases, however, in which the communication between the aorta and pulmonary

artery is wide, that division as contrasted with simple ligation, offers the patient the best assurance against recanalization. In the easy case, in which the ductus is long, ligature may hold out almost as bright a prospect of permanence as division with respect to recanalization. But if division is necessary to protect against the possibility of rechanneling following ligation in continuity, why merely ligate in the easy case? There have been 69 divisions of the ductus in this series with 1 death. Recanalization has not occurred.

COMPLICATIONS

Hemorrhage. In 1 instance in this series, one of us (O.H.W.) fell afoul the inherent difficulties of division. It concerned a large woman (Univ. Hosp. No. 780,697) of 31 years with subacute bacterial endocarditis, auricular fibrillation and cardiac decompressation and a large patent ductus. She was a precarious operative risk and had been having chills and fever accompanied by dyspnea, anorexia, and weight loss of 6 months' duration. There had also been episodes of pulmonary infarction with hemoptysis and chest pain. The auscultatory cardiac findings were typical of a patent ductus. On examination here, multiple petechial hemorrhages were noted in the skin. The patient was cyanotic and dyspneic. The vital capacity was 0.9 liter; there was blood in the urine and the blood urea nitrogen was 90 milligrams per cent. Under penicillin therapy, 3,000,000 units per day for 4 weeks, the fever which had ranged between 100 and 101 degrees gradually subsided. The patient improved with digitoxin, a salt free diet, and small frequent blood transfusions. The advisability of undertaking operation was debated and was undertaken as a last resort measure, no one feeling any real enthusiasm for the procedure. At operation a very broad ductus, measuring more than 30 millimeters in width was found. The dissection about the ductus was tedious and difficult occupying more than 2 hours. It was accomplished, however, without too much difficulty, the illuminated dissector proving a real help. The urge to terminate the operation by ligation was real. Mindful of the circumstance that it is in just such cases that the greatest hazard of recanalization lies, division was done. The aortic side of the ductus was dealt with without difficulty. When the stick-tie ligature behind the lower clamp on the pulmonary artery side was drawn up, however, the vessel tore; the bleeding was arrested by digital pressure without too much difficulty and a small hemostat was substituted for digital compression at the site of leak; when, however, ligature of the bleeding point was attempted by placement of another matress suture, the pulmonic end of the ductus tore again. This procedure was repeated four times before hemostasis was complete. It had become quite obvious that a granulomatous process probably involved the vessel wall. Meanwhile the blood loss had been large but had been replaced adequately by blood run in through two intravenous infusion needles placed prior to operation. Fibrillation of the auricles set in followed by cardiac arrest. Ventricular contractions were restarted several times by cardiac massage and epinephrine, but effective, continued ventricular contractions could not be induced. At autopsy the heart weighed 715 grams. On the aortic side of the ductus in which no special difficulty had been encountered in the operation "3 or 4 tiny friable vegetations measuring 1 millimeter in diameter were found." In the pulmonary trunk there were several cracks in the intima and there was "a large patch of vegetation on the anterior wall of the pulmonary trunk which extended to the left pulmonary artery where it surrounded the origin of the ductus."

The difficulty encountered at operation after division of the ductus is quite understandable in the light of the postmortem findings.

Trying difficulties with hemostasis occurred in only 1 other instance. It concerned a girl of 14 years with pallor in whom a suspicion of subacute bacterial endocarditis had been entertained but not established. She, too, had a broad, short ductus; however, the vessel wall held sutures better than the patient referred to previously and the situation though critical turned out happily.

Fever. In a young child of 5 years, who had been febrile intermittently for months prior to operation, running a fever as high as 101 to 102 degrees Fahrenheit daily in the afternoon,

fever continued intermittently for about a month after operation, affording us serious concern lest a small cottonoid sponge had been lost in the wound. The fever eventually disappeared entirely. During convalescence too probably, this patient's fever was caused by subacute bacterial endocarditis, which diagnosis had not been established definitely prior to operation.

Pleural fluid. Aspiration of pleural fluid has been necessary in approximately one-third of the patients. Amongst the adults in the series, accumulation of pleural fluid has been more frequent than in children. More than one aspiration has been unusual.

Temporary paralysis of arm. One patient in the group sustained a temporary paralysis of the muscles of the left hand and forearm, supplied by the brachial plexus, undoubtedly owing to inadequate padding of the left axilla.

Cardiac arrest. One other patient for whom operation was undertaken for a patent ductus, but not completed because of temporary cardiac arrest, bears special mention. She was a beautiful child of 4 years (Univ. Hosp. No. 775869). The chest had barely been opened when cardiac arrest occurred. Such grim and tense moments upset the quiet but serious atmosphere of an operation progressing satisfactorily. Differences of opinion and attitudes toward causation as well as mode of management are understandable in such trying conditions. Valuable time was lost in this instance through the insistence of the anesthetist that the vagus nerve should be injected with procaine first; that procaine should be injected into the pericardium and then into the ventricle. All these things were done, the heart muscle being massaged meanwhile, blood also being dripped into an ankle vein. The anesthetist's uneasiness relating to the use of epinephrine concerned his fear that, inasmuch as cyclopropane anesthesia had been employed, ventricular fibrillation would be induced by epinephrine. One cubic centimeter of epinephrine was then injected into the left ventricle. Effective cardiac contractions began directly. A few minutes later an additional 0.5 cubic centimeter of 1–1000 dilution of epinephrine was given again. The second period was of only a few minutes' duration. The chest wall was closed without attempting dissection or exposure of the ductus. As the final skin sutures were placed, cardiac arrest occurred again, oxygen only having been administered by inhalation meanwhile. The chest was opened again and the heart was massaged followed by reinjection of 0.5 cubic centimeter of epinephrine with immediate commencement of ventricular contractions. The anesthetist's record indicated that no blood pressure was obtainable for 45 minutes in the first long period of cardiac arrest.

The cause of the cardiac arrest in this patient has not been uniformly agreed upon. The concensus, however, is that it probably was owing to too high a concentration of carbon dioxide in the alveolar mixture. In other words, anesthetists are sorely in need of agents which will tell them more definitely and promptly from time to time in operations, what the likely concentration of carbon dioxide is in the alveolar air.[1]

The more remote occurrences in this patient are equally as interesting. For several days the patient was unconscious, responding only to painful stimuli; for a period of almost a week she also was oliguric, excreting only 15 to 60 cubic centimeters of urine a day with a low specific gravity. During this time she was weighed twice daily, enough 50 per cent glucose solution being given to meet her caloric requirements. After a week's time she showed signs of rousing, accompanied by manifest evidences of irritability. Within 10 days of operation it was apparent that she was aware of the presence of people about her. It was evident that she could hear them. Her speech at this juncture was hesitant; she could repeat words and terms of endearment seemed to elicit a suggestion of an earlier familiarity with them; that her memory of certain previous experiences was retained was evident 3 weeks after operation when asked one morning if she could sing, she sang sweetly and without faltering or hesitation: "Jesus loves me, this I know, for the Bible tells me

[1]As a result of this experience, work is now in progress in this clinic with the help of Dr. A. O. Nier of the Department of Physics and Dr. Allan Hemingway of the Department of Physiology to develop a portable spectrograph to aid the anesthetist in determining the concentration of CO_2 in the alveolar air during operative procedures.

so." Hearing, sense of smell and speech appeared to return in that order. While we waited from day to day with mixed feelings of hope and despair for encouraging signs of improvement it had been urged that steps be taken to commit the child to an institution—a suggestion which the parents as well as the surgeons resisted. Four to 5 weeks after operation it was obvious that the child could discern darkness from light. Her speech improved gradually and the movements of her extremities became more co-ordinated. Nine weeks after operation she was dismissed from the hospital returning for occasional observation in the outpatient clinic. Ability to differentiate colors and to distinguish circles from triangles and other evidences of returning vision appeared months after the cardiac arrest. During the past school year, the patient made her way to school unaided.

SUMMARY

In all, operative division of the ductus has been done in 69 consecutive cases.[1] The only death in the series concerned a patient of 31 years with subacute bacterial endocarditis, auricular fibrillation, and severe cardiac decompensation in whom a granulomatous plaque beneath the pulmonic end of a broad ductus made ligature difficult after division of the ductus. Touroff's suggestion that ligature is a wiser expedient than division in such instances is borne out in this experience.

A technique for dissection and division of the ductus, constituting essentially minor variations of the technique described by Gross is detailed herein.

The average postoperative hospital stay, save for the patient with a complication, has been less than a week

[1]At the present time (August 10, 1948), 8 additional patients have been operated upon without complication. Ligature rather than division was done in one of them, Mrs. M. M. University Hospital No. 786,315, aged 33, for this patient had a condition in many respects very much like that reported in the instance of Mrs. O. L. (780,697) above. Ligature was done on February 25, 1948 and no evidence of recanalization has appeared.

REFERENCES

1. Blalock, A., and Taussig, H. B. J. Am. M. Ass. 1945, 128: 189–202.
2. Idem. Surg. Gyn. Obst., 1946, 82: 113.
3. Crafoord, C., and Nylin, G. J. Thorac. Surg., 1945, 14: 347.
4. Cutler, E. C. Personal communication, February, 1935.
5. Fahr, G. E. Personal communication, February, 1935.
6. Gross, R. Ann. Surg., 1939, 110: 321.
7. Idem. Surg. Gyn. Obst., 1944, 78: 36.
8. Idem. J. Thorac. Surg., 1947, 16: 314.
9. Discussion of papers of J. C. Jones and Robert Gross at 1946 meeting of American Thoracic Association. J. Thorac. Surg., 1947, 16: 320.
10. Shapiro, M. J. Personal communication.
11. Touroff, A. S. W. Discussion (9).

FRACTURES OF THE UPPER END OF THE RADIUS AND ULNA

FRANK D. DICKSON, M.D., F.A.C.S., Kansas City, Missouri

A FRACTURE into the elbow joint is always a threat to the usefulness of this articulation because serious impairment of function so frequently results. The importance of the elbow joint need not be elaborated upon, as it is common knowledge that the loss of, or serious interference with, flexion and extension or pronation and supination, movements which take place in this joint, may interfere with the ability to earn a livelihood and the performance of many acts necessary to satisfactory and gracious living.

Fractures into the elbow joint numerically comprise an important group, as they make up a considerable portion of the fractures which must be dealt with both in private practice and in large fracture clinics. Supracondylar fractures are the most frequent fractures of childhood and adolescence, and comminuted fractures of the lower end of the humerus are increasing in frequency in the youth and adult groups largely because of the reprehensible habit of driving an automobile with an elbow projecting from the window, a habit which is quite prevalent today. When to these two groups are added fractures of the upper end of the radius and ulna, it is evident that there is a rather formidable list of fractures which may be expected to result in some permanent impairment of the function of the elbow joint. Philip Wilson in the Fracture Oration of 1932 under the title, "Fractures and Dislocations of the Elbow," discussed injuries to this region in a very comprehensive way and left little of importance to be added. The chief emphasis in that analysis, however, was placed upon fractures of the lower end of the humerus; this presentation which deals only with fractures of the upper end of the radius and ulna should serve to bring into focus the part played by fractures of these elements of the elbow joint in the production of pathology, which causes impairment in its function.

Anatomically, by the term "elbow joint" is meant the articulation between the lower end of the humerus above and the ulna and head of the radius below (Fig. 1). The articulation between the ulna and the head of the radius forms the superior radioulnar joint, which does not belong to the elbow joint proper. However, the movements of flexion and extension, which take place in the elbow joint, and the movements of pronation and supination, which take place between the radius and the ulna centered in the superior radioulnar joint, are so intimately related that from a functional point of view these two joints must be considered as one. The intricate movements the forearm and hand are called upon to carry out are possible only through coordination of the movements of flexion and extension and pronation and supination, and this coordination depends not only upon the proper alignment of the ulna and the head of the radius with the lower end of the humerus but also upon proper alignment between the head of the radius and the ulna. Any disarrangement in these alignments, no matter where it occurs, can not fail to impair function in the elbow joint either in the direction of flexion and extension or pronation and supination or both. It is with those fractures of the upper end of the radius and ulna which interfere with the proper alignment of the bones which comprise the functional elbow joint that this discussion is concerned.

The fractures to be considered are: (1) fractures of the head of the radius, (2) fractures of the olecranon, (3) fractures of the upper end of the ulna with dislocation of the head of the radius (Monteggia fracture).

FRACTURES OF THE HEAD OF THE RADIUS

Fracture of the head of the radius results from a fall on the outstretched hand. When such an accident occurs, the elbow is almost

[1]Fracture oration presented before the Clinical Congress of The American College of Surgeons, New York, September 8-12, 1947.

completely extended and the radius pronated so that the anterolateral section of the head of the radius is driven with considerable violence against the capitellum of the humerus. The damage sustained by the head of the radius depends upon the force of the impact; usually it is possible to differentiate three types of fracture of the radial head by roentgenogram: (1) a fissure fracture with no or mild displacement; (2) a marginal fracture with displacement of a sector of bone; (3) a comminuted fracture involving most of the head of the radius.

Fracture of the head of the radius should be readily diagnosed, as the symptoms complained of are classic; these are tenderness over the head of the radius on palpation, limitation of extension of the elbow joint with onset of acute pain if extension is even mildly forced, and limitation of pronation and supination with production of pain if these movements are persisted in. While the symptoms enumerated are common to all three types of fracture of the head of the radius, the form of treatment indicated varies with the type to be dealt with; this fact must be held constantly in mind in planning the management of radial head fractures.

Treatment. It is important to remember that a fracture of the head of the radius is not the trivial injury it may appear and that intelligent treatment based on clear roentgenograms carefully studied is demanded if permanent impairment of elbow joint function is to be avoided. Furthermore, injury to the cartilage of the capitellum and even fracture of the capitellum, the result of the impact of the head of the radius against it, and ligamentous damage are complications that not infrequently are associated with this fracture, and such possible complications must be considered in any plan of treatment decided upon. For clarity, the treatment of each type will be discussed separately.

Fissure fractures (*Fig. 2*). The injury is a subperiosteal crack which separates slightly a sector of bone from the radial head, usually from its outer border. In young individuals the injury may consist in a tilting of the head on the neck. Although the displacement in this type of fracture is minimal, if permitted to persist an incongruence between the head of the radius and the capitellum will develop and result in permanent limitation of extension and pronation and supination. Such fractures should be treated by supporting the elbow at a right angle in a sling for a week to 10 days to allow the traumatic reaction to subside; at the end of this period the sling should be removed four or five times a day and active flexion and extension and pronation and supination carried out by the patient. There should be no passive manipulation or forcible stretching at any time as such maneuvers are likely to cause a serofibrous reaction and the formation of calcareous deposits in the capsule of the joint with permanent impairment of function. On the other hand active movements, which the patient himself controls, will be guarded and so unlikely to be forced sufficiently to cause an unfavorable reaction. The purpose of daily movement is to mold the distorted radial head to the capitellum while the fracture is still in a plastic state; by so doing even if an anatomical reduction is not secured, a satisfactorily functioning joint results. At the end of 3 weeks, the sling may be discarded and use continued until healing is complete; this usually requires from 8 to 10 weeks. A few degrees of limitation of extension will usually persist, but this is not incapacitating.

Marginal fractures with displacement (*Fig. 3*). In this type of fracture of the head of the radius, a sector of bone, usually from the lateral-anterior part of the head, is depressed and impacted or tilted out of position, or completely separated from the main fragment. When the fragment is impacted or tilted out of place but still in contact with the remainder of the head, conservative treatment is indicated. Such conservative treatment is the same as that used in type one, namely immobilization of the elbow at right angles for 10 days to 2 weeks, preferably in a posterior plaster mold in this fracture for more complete immobilization. At the end of this time the splint may be replaced by a sling and active flexion and extension and pronation and supination movements carried out by the patient five or six times daily. Again it should be emphasized that passive manipulation and forcible stretching are harmful and may lead to permanent interfer-

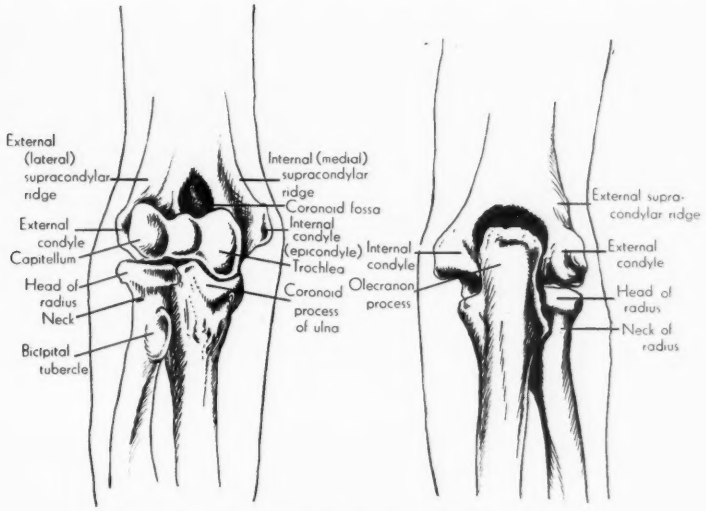


Fig. 1. The elbow and superior radioulnar joints.

ence with function. The same molding of the distorted head to the capitellum is brought about by early guarded movements in this fracture as in type one, and an essentially normal range of joint motion will result.

When the fractured-off sector is completely separated from the main fragment (Fig. 4), conservative measures should be abandoned and surgery resorted to as ossification of the intervening hematoma produces an irregularly-shaped head which will not articulate properly with the capitellum or the ulna and limitation of both flexion and extension and pronation and supination will follow. The surgery carried out depends upon the degree of damage suffered by the radial head. If the fragment is but a small sector and the remainder of the head is intact, simple removal of the loose fragment is all that is necessary. If the fractured sector comprises a large segment of the head (Fig. 5) or if there is any degree of comminution present, the entire head should be resected as arthritic changes will certainly develop later.

When dealing with fractures falling in type 2, it is necessary to make the decision early as to whether they should be treated conservatively or by surgery. If arthrotomy is to be performed and the fragment removed or the head resected, it should be done within 10 days of the injury; delay for several weeks will almost invariably give a less satisfactory result with definite impairment of function. As in type 1, some limitation of extension and perhaps slight limitation of pronation and supination are to be anticipated.

Comminuted fracture of the head of the radius (*Fig. 6*). In this type the head of the radius is broken up into a number of fragments which lie loose in the joint or the head is entirely fractured off and completely turned on itself. Conservative measures have no place in the treatment of such fractures, as dense adhesions between the fragments and the capsule rapidly form. Excision of the entire radial head is necessary if joint function is to be preserved (Fig. 7). The optimum time for surgery is within 7 to 10 days of the injury, for if surgery is delayed for several weeks or months, limitation of joint motion will already have developed, and late removal of the head seldom improves the result.

When the radial head is to be removed, the incision should be placed over the head of the radius posterior to the extensor muscle mass where the field is almost bloodless. The neck of the radius should be cut across cleanly with an osteotome at the level of the upper border of the orbicular ligament. The raw surface of

the neck should be covered with a flap, comprised of stripped back periosteum or flaps dissected from surrounding soft tissues, to seal it off and to prevent proliferative changes at this point. The most frequent error made is failure to resect far enough distally. When this error is made, the expanded part of the neck is left behind and adhesions between it and the ulna frequently form and limit pronation and supination. Placing the incision too far forward brings it near the posterior interosseus nerve, damage to which will result in wrist drop.

FRACTURES OF THE OLECRANON

Fractures of the olecranon may be caused by direct violence, such as a fall or blow on the tip of the elbow, or by indirect violence in the form of forcible flexion of the elbow against the strong resistance of the powerful triceps muscle. Some fractures of the olecranon result in slight or no separation of the fragments (Fig. 8); such fractures cause little disturbance in the elbow and present no problem in treatment. When, however, there is separation of the fragments ot even as little as one-fourth inch, a definite problem in treatment is involved (Fig. 9). With displacement of the proximal fragment the triceps tendon, which is attached to it, is relaxed and loses its power to extend the elbow actively. Permanent relaxation of the triceps tendon, which must occur unless the fragments are brought into contact and a firm, bony union secured, will result in continuing weakness of active extension of the elbow, which prevents reaching for objects above the shoulder level and weakens the ability to push against resistance. If the fragments are not brought into apposition and a fibrous union occurs, degenerative arthritic changes in the articular cartilage of the elbow joint may be anticipated, and limitation of flexion and extension will occur in a very considerable percentage of cases. Even if bony union takes place in spite of separation of the fragments an incongruence of the joint surface develops and serious limitation of flexion and extension is the usual outcome. It may be stated, then, that fractures of the olecranon like fractures of the head of the radius can not be considered to be trivial injuries but on the contrary may lead to serious disability in the elbow joint.

Treatment. There are two objectives to be sought for in treatment of fractures of the olecranon: (1) the restoration of normal length and tension of the triceps muscle so that it may function properly; (2) the securing of a normal contour of the upper end of the ulna, which must articulate accurately both with the trochlear surface of the humerus and the olecranon fossa, into which the olecranon fits when the elbow is extended, if normal function is to be restored. Unless both these objectives are attained, normal or even useful elbow function will be jeopardized.

Fractures of the olecranon without separation can be dismissed with brief comment. If flexion of the elbow does not cause separation of the fragments, the elbow should be treated by immobilization in a posterior plaster mold in right angle flexion. If flexion causes even the slightest separation, the fracture should be treated in extension in an anterior plaster mold extending from the axilla to the palm. If the extended position is necessary, it is desirable to initiate flexion movements as early as possible, but such movements should not be started too early. Many advise starting flexion in 3 weeks; our experience, however, has been that this is too early and that 5 weeks is as soon as flexion exercises should be carried out. Separation of the fragments with disastrous results has occurred in several cases which have come under our observation in which early motion had been insisted upon. Recovery of motion should be achieved by active movements carried out by the patient. Passive movements and forcible stretching are contraindicated because of the danger of setting up a fibrosis in the capsule. Ample time should be allowed for recovery, as some limitation of movement may persist for 8 or 10 months.

Fractures of the olecranon with separation of the fragments present quite a different problem in treatment. Restoration of length and tone to the triceps muscle and proper modeling of the upper end of the ulna must be attained to insure a satisfactory outcome. If extension of the elbow and manipulation of the proximal fragment do not result in perfect apposition, surgery must be resorted to in practically all cases. One other method of closed reduction

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 2. Fissure fracture of the head of the radius; no displacement. (Type 1)

Fig. 3. Marginal fracture of the head of the radius. Type 2 suitable for conservative treatment.

Fig. 4. Marginal fracture of the head of the radius, type 2; fractured fragment should be removed.

Fig. 5. Marginal fracture of the head of the radius, type 2; head should be resected if fractured segment is large or comminution is present.

Fig. 6. Comminuted fracture of the head of the radius, type 3; entire head should be resected if joint function is to be preserved.

and immobilization may be employed when the olecranon fragment is large (Fig. 10). In this method the fragment is transfixed with a Steinmann pin and levered into position. After reduction has been accomplished, the pin is driven down into the ulna a sufficient distance to anchor firmly the fragment in position. A plaster cast should then be applied with the elbow at right angles. The end of the Steinmann pin is allowed to project through the cast and fixed in position with a few turns of plaster. When this method is used, the alignment of the fracture should be checked by fluoroscope or roentgenograms before the pin is driven home in the ulna. Our experience indicates that the pin should be driven into the ulna in such a way as to engage the cortex of the bone rather than pass down in the medullary canal, as better fixation is secured. Plaster fixation should be maintained for 5 weeks, after which time the pin may be removed and active exercises started. This form of treatment has given satisfactory results in 5 cases in which it was used and unsatisfactory results in 3 cases. The method is not without drawbacks and should be used only in selected cases; frequent check of position by roentgenogram should be made during the first 2 weeks. The

Fig. 7a.

Fig. 7b.

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 7. a, Head of radius fractured completely off; b, head has been resected at correct level.

Fig. 8. Fracture of olecranon without displacement.

Fig. 9. Fracture of olecranon with displacement.

Fig. 10. Steinmann pin used to reduce and fix a fracture of the olecranon. The head of the radius has been resected.

Fig. 11. Unsatisfactory result of Steinmann pin fixation in case shown in Figure 10. Arthritic changes and definite limitation of motion; an unsuitable case because of associated fracture of the head of the radius.

unsatisfactory results were those in which arthritic changes occurred with definite limitation of motion (Fig. 11).

Practically all fractures of the olecranon with separation are best treated by surgery since active extension of the elbow can be expected only if the triceps is re-united to the ulna without lengthening of its tendon and normal flexion and extension only with accurately fitting joint surfaces in the hinge between the ulna and the trochlea of the humerus and accurate seating of the olecranon in the olecranon fossa. The normal length and tone of the triceps can be restored by one of two surgical procedures: (1) open reduction of the fracture with the use of internal fixation so that bony union in perfect position will result; or (2) by excision of the olecranon fragment and reattachment of the triceps tendon with its lateral aponeurosis to the upper end of the ulna.

When open reduction is chosen, fascia lata should be used as the fixation material. Fine stainless steel wire may be used, but screws and nails are less desirable because of the early and late tissue reaction which they may excite. The fracture is exposed and cleaned of all interposing tendon fibers which may have fallen between the fragments and interfere with bony contact. A hole should be drilled transversely in the distal fragment of the ulna and a suture passed through the drill hole and around the proximal fragment, engaging the entire triceps insertion in which it is buried (Fig. 12). This suture should cross over the fracture so that

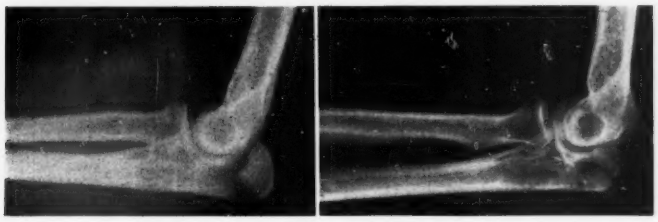


Fig. 12.

Fig. 12. Open reduction of fracture of the olecranon with fascia lata suture used, single drill hole.

Fig. 13. Open reduction of fracture of the olecranon; stainless steel wire used as suture. Crossing suture to prevent displacement is shown as well as extra suture running from fragment to fragment.

Fig. 14. a, Compound, comminuted fracture of the olecranon; b, wire and single screw used for fixation because of comminution, with malalignment and limitation of motion; c, later resection of the olecranon with restoration of practically normal range of motion.

a b c

Fig. 13.

a b c d

Fig. 14.

when tied it will approximate the fragments and prevent tilting and lateral displacement. If the olecranon fragment is large, it is better to drill a tunnel through each fragment and add a second suture passing directly from drill hole to drill hole (Fig. 13). The elbow should then be gently flexed to about a right angle and the position of the fragments carefully checked to see that accurate reduction is maintained. The elbow should be immobilized in plaster at right angles for 5 to 6 weeks. Active movement is carried out as in the closed method.

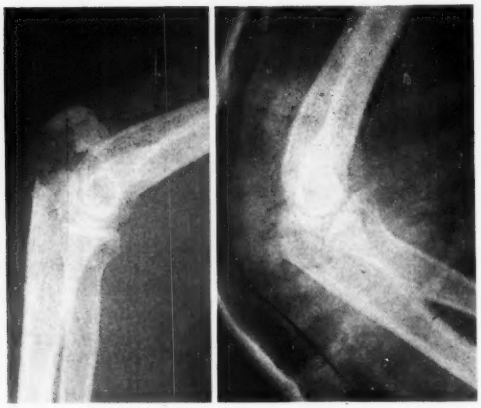


Fig. 15. Primary resection of proximal fragment. Normal function in 8 weeks.

Excision of the olecranon fragment is, in our experience, a much simpler and more certain method of treating fractures of the olecranon with separation than is open reduction. Even with accurate reposition, malalignment of the proximal fragment may develop in the course of healing (Fig. 14). This displacement may prevent the tip of the olecranon from seating properly in the olecranon fossa, and limited extension follows. Degeneration of the articular cartilage on the ulna and even on the trochlea may take place, the result of the trauma suffered at the time of injury, and such degenerative changes produce a traumatic arthritis in the elbow joint with limitation of flexion and extension although alignment may be perfectly maintained. When the olecranon fragment is excised, all danger of any incongruence between the olecranon and the olecranon fossa is removed, and the danger of traumatic arthritis due to degenerative changes in the articular cartilage of the ulna is eliminated. Return of normal flexion and extension movements takes place rapidly, and the convalescent period is markedly shortened (Fig. 15).

The essential part of the operation is not the excision of the olecranon fragment but reattachment of the triceps tendon. The fragment should be shelled out by close, sharp dissection, preserving all attachments of the triceps tendon. Two drill holes should be made in the proximal end of the ulna. Mattress sutures of fascia lata are placed in the triceps tendon and passed through the drill holes in the ulna, firmly anchoring the tendon to bone. Additional fixation is secured by suturing with catgut the lateral margins of the triceps tendon to the fascia on each side of the ulna. The elbow should be immobilized in plaster at right angles for 10 days to 2 weeks, and then active exercises should be carried out to restore use which will usually return rapidly. There is no danger of forward displacement of the ulna even if quite a large fragment must be removed, as the strong triceps muscle prevents this. Only failure to reattach the triceps tendon properly and adequately will allow forward displacement to occur. We have found resection so satisfactory that it is used routine-

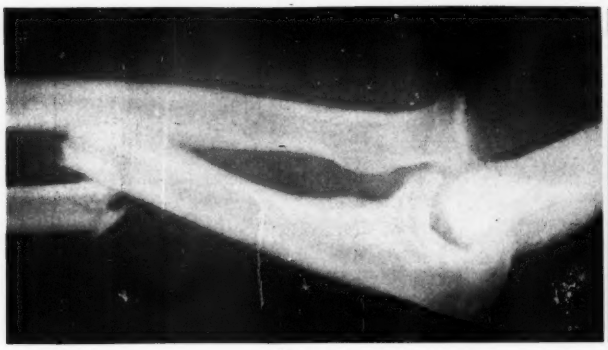


Fig. 16.

Fig. 16. Typical Monteggia fracture of the ulna with dislocation of the head of the radius.

Fig. 17.

Fig. 17. Atypical Monteggia fracture, really an anterior dislocation of the elbow.

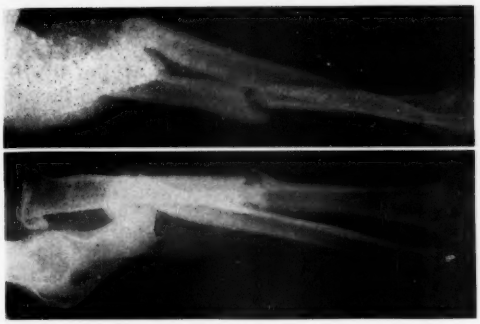


Fig. 18. Unreduced Monteggia fracture with extensive disability.

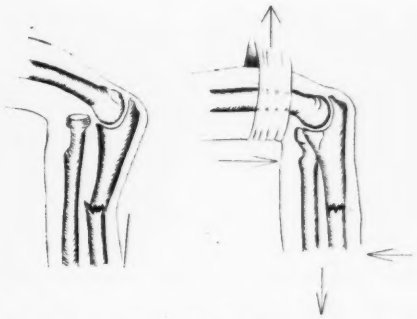


Fig. 19. Diagram of method of closed reduction of Monteggia fracture.

ly in our clinic unless there are complicating factors which make it undesirable.

MONTEGGIA FRACTURES

Fracture of the upper end of the ulna with dislocation of the head of the radius, first described by Monteggia a century ago, is one of the most disastrous fractures which occurs about the elbow joint so far as impairment of elbow function is concerned. Statistics indicate that in approximately 90 to 95 per cent of cases permanent disability of a high grade follows this fracture. The typical Monteggia fracture (Fig. 16) of the ulna occurs 3 to 4 inches below the olecranon, but the line of fracture may lie closer to the joint (Fig. 17). The solution in the continuity of the ulna is complicated by rupture of the orbicular ligament and dislocation of the head of the radius. Satisfactory reduction and maintenance of reduction of the fracture of the ulna are difficult

Fig. 20. The result of inadequate internal fixation; wire loop failed to hold fracture in place.

so that malunion is frequent, and extensive damage to the orbicular ligament often makes it impossible to maintain the head of the radius in position after it is reduced. Malunion of the ulna and permanent dislocation of the head of the radius mean an elbow joint in which both flexion and extension and pronation and supination will be permanently limited and to a serious extent (Fig. 18).

Treatment. A Monteggia fracture of the usual type is reduced by flexing the elbow, apply-

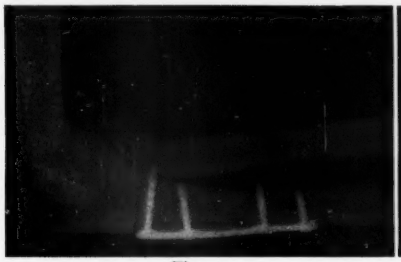


Fig. 21.

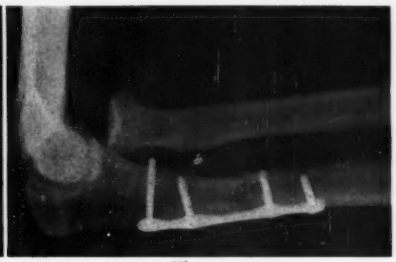


Fig. 22.

Fig. 21. Adequate fixation of fracture of ulna; head of radius apparently reduced.
Fig. 22. Same fracture as shown in Figure 21, 2 weeks later showing redislocation of head of the radius.

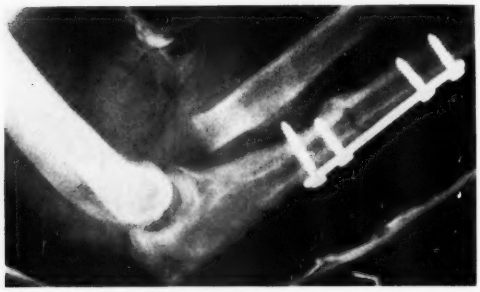


Fig. 23. Late resection of the head of the radius in a Monteggia fracture with practically normal function.

ing traction, and manipulation (Fig. 19). Unfortunately, these maneuvers give a satisfactory reduction of the fracture of the ulna and replacement of the dislocation of the head of the radius in comparatively few cases, and in these there is a strong tendency toward displacement. Very few Monteggia fractures are successfully reduced by manipulation, and open reduction with internal fixation is demanded from the start. The fracture should be exposed, accurate reduction secured, and the fragments immobilized with an adequate bone plate (Fig. 20). Perfect reduction of the ulnar fracture will, as a rule, bring about replacement of the dislocated head of the radius (Fig. 21). If the head of the radius fails to reduce, it should be manipulated into place; it should not be exposed and open reduction and repair of the orbicular ligament undertaken. Open replacement of the dislocated radial head if carried out at the same operation as plating of the ulna almost invariably leads to ankylosis or limitation of motion in the upper radioulnar joint because of ossification about the head and neck of the radius, which usually follows. Watson-Jones considers this ossification to be due to the deposit of calcium in the hematoma disseminated into the muscles and ligaments by surgical interference. If the displacement of the head of the radius can not be corrected by reduction of the ulna and manipulation, it should be allowed to remain displaced, and 2 or 3 months later the head should be resected. Contrary to what occurs in fractures of the head of the radius, late removal of the dislocated radial head gives excellent function as regards flexion and extension and pronation and supination. In a certain number of cases, the head of the radius will replace when the ulna is brought into alignment, but within a few days or a week or two, it will redislocate because the orbicular ligament fails to repair itself (Fig. 22). When this complication occurs, it is best to do nothing about it for 2 or 3 months and then resect the radial head (Fig. 23). There are many with wide fracture experience, who prefer to reconstruct the orbicular ligament rather than resect the head of the radius; if this is done it should be postponed for at least 2 months as is resection of the head and for the same reason. In our experience, late resection of the radial head has given more satisfactory results than attempts to reconstruct the orbicular ligament, as it is rarely possible to anchor the head of the radius securely in place by an artificial ligament, and the radioulnar joint is so relaxed that it may be unreliable, painful, and later develop arthritis.

The elbow joint from childhood is vulnerable to injury. The mechanics of the functional elbow joint are so complex that any injury which interferes with the proper alignment of its component parts can cause impairment of function of serious degree. Because this is so, fractures which involve the upper end of the radius and ulna, important elements in the joint, demand careful appraisal and the selection of that form of treatment which will insure restoration of the most advantageous relations between the articular surface of the ulna, the head of the radius, and the lower articular surface of the humerus. Anatomical alignment is important, but a satisfactorily functioning elbow joint is more so, and restoration of function must be the aim of treatment. The first step to this end is understanding that no fracture which enters the elbow joint is a trivial injury but one which carries with it the possibility of permanent impairment. The second step is never to overlook the susceptibility of the elbow joint to form adhesions and so avoid in the after treatment of elbow fractures, including those of the upper end of the radius and ulna, the use of passive motion and forceful manipulation, which promote the formation of adhesions, and these always result in limitation of movement in one or more directions with varying degrees of disability.

ONE HUNDRED CASES OF CONGENITAL ABSENCE OF THE VAGINA

ALLEN L. BRYAN, M.D., JOSEPH A. NIGRO, M.D., and
VIRGIL S. COUNSELLER, M.D., F.A.C.S., Rochester, Minnesota

THE primary purpose of this article is to compare the various methods of surgical treatment for congenital absence of the vagina. During the course of time many procedures have been utilized with varying degrees of success, but only relatively recently has an entirely satisfactory method been employed which is simple, entails minimal morbidity and mortality, and produces a high percentage of good results.

We are including 14 operations done according to the Baldwin technique, 1 according to the Falls method, 1 of iodoform gauze packing, 70 McIndoe procedures in which split-skin grafts are employed and 14 operations performed according to the technique popularized at the clinic by one of us (V. S. C.), which consists of simple dissection and insertion of a mold. Data on 76 of these cases were presented by the senior author (V. S. C.) at the meeting of the American Medical Association at Atlantic City, New Jersey, June 9 to 14, 1947.

EMBRYOLOGY

Development of the vagina varies from partial to total. This structure is derived from the (1) muellerian ducts (18, 32), (2) wolffian ducts, and (3) urogenital sinus (29, 37–40, 51). Numerous microscopic sections made on human embryos during growth have materially aided embryologists. At 8 millimeters the muellerian ducts appear as an evagination of the celomic cavity lateral to the upper portion of the wolffian ducts. The caudal portion of the muellerian ducts forms a tube with a solid tip which burrows itself through the mesenchyme of the urogenital fold crossing the wolffian ducts anteriorly and at the caudal end of the mesonephros. At 30 millimeters the caudal tips of the muellerian ducts fuse and reach the posterior wall of the urogenital sinus, pushing it forward and forming the muellerian tubercle. With the distal fusion of the muellerian ducts, the uterovaginal canal is formed. The wolffian ducts have kept pace with the muellerian system but, at 56 millimeters, begin showing signs of involution. Approximately at this time there is a great intermingling of cells of the urogenital sinus, wolffian ducts, and muellerian ducts, and here is where controversy persists as to what group of cells proliferates to predominate in the formation of the vagina. At 63 millimeters the muellerian tubercle gives way to the bilateral sinovaginal bulbs formed by the evagination of the posterior wall of the urogenital sinus. The growing of the sinovaginal bulbs and the transformation of the columnar epithelium to stratified epithelium of the lower portion of the uterovaginal canal results in the formation of primitive vaginal plate. The vaginal plate increases in size and proliferating cells invade the surrounding mesenchyme. The epithelial activity begins at the caudal end. This proliferation forms a solid vaginal cord. The cells in the center of the solid cord undergo involution and desquamation, thereby forming the vaginal canal, which first appears in embryos of 150 to 200 millimeters trunklength; this canal communicates with the cervical canal above and the hymenal foramen below (43).

From the Division of Surgery, Mayo Clinic and Mayo Foundation.

SURGICAL PROCEDURES USED IN RECONSTRUCTING AN ARTIFICIAL VAGINA

Bowel transplants. In this country, when a portion of bowel is to be used as the new artificial vagina, the Baldwin technique has been favored most. In 1904 Baldwin (3, 4) described a method for using the ileum as a transplant but did not have a chance to try it until 1907. The method proposed was to excise a loop of ileum 10 inches long (25 cm.) and to reunite the bowel by an end-to-end anastomosis. He then dissected between the bladder

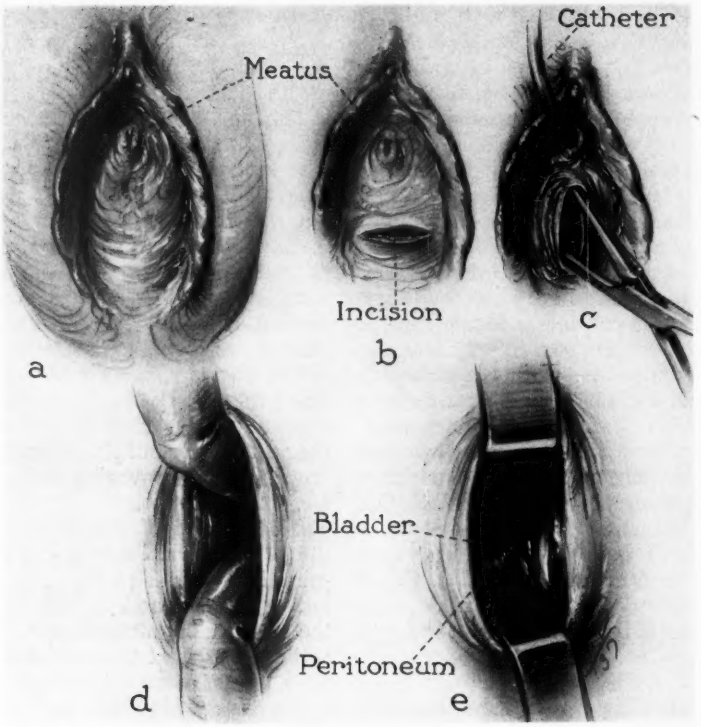


Fig. 1. Construction of an artificial vagina. a, Absence of evidence of vagina; b, transverse incision at new site of vagina, well away from the urethra; c, tissue separated by blunt forceps to locate the fascial plane between the bladder and rectum; d, bladder and rectum being carefully separated with the fingers; e, peritoneum of the cul-de-sac being elevated by retraction to secure depth for a new vagina. (From Counseller, V. S. Congenital anomalies with particular reference to cryptorchidism, hypospadias and congenital absence of vagina. *J. Michigan M. Soc.*, 1938, 37: 689–697, Fig. 4, p. 696.)

and rectum, using a perineal approach, pulled the middle of the isolated loop downward, attached the upper end of the loop around the cervix and closed the other end. The abdomen was then closed. With the patient in the lithotomy position and the loop of bowel held in a forceps, the bowel was opened up, cleansed, each limb was packed with iodoform gauze and the edges of the bowel were attached to the surrounding hymenal margins. After 2 weeks a clamp was placed on the double-barreled septum converting the two loops of bowel into one canal. In 1910, this procedure was modified by Mori, who used only one loop of bowel sutured to the vaginal introitus.

Previously, the rectum had been employed in repair of this condition as reported by Sneguireff in 1892, who made an incision from the coccyx to the anus and separated the rectum from the coccyx, which was excised. The intestine was ligated in two places and divided. The superior segment was sutured to the right of the coccygeal region and the inferior segment was brought down and its upper end closed. Two weeks later a second stage was done, in which the perineum was incised and the rectal mucous membrane was sutured to the adjacent parts. In 1910, Popow and in 1911, Schubert utilized methods similar to those used by Sneguireff.

Labial grafts. The first to use labial grafts to form an artificial vagina was Jewett in 1904, but Graves popularized this method in 1908, using two labial flaps and two thigh flaps over a glass form. When the skin pouch was almost completely sutured, the glass form was removed and the flaps invaginated and sutured to the depths of the vault. Davis and Cron modified Graves's method by using only labial flaps and by making their original perineal incision vertically rather than transversely. Falls in 1940 cut a disc 2 to 3 centimeters in diameter around the introitus, then undercut the edges and pushed the disc back by blunt dissection. Four skin flaps from the vulval opening were taken and their free end was sewed to the edges of the disc. This skin-lined cavity was packed with gauze daily with moderate pressure until healing was complete. Meigs suggested tunneling between the bladder and rectum and then leaving a mold in place for 6 to 12 months, after which internal grafting according to the Graves method is carried out.

Grafts from thigh. In 1900 Beck reported use of skin flaps from the thigh after he had opened a tract between the bladder and rectum using both abdominal and perineal incisions. All the dissection was done extraperitoneally, and after the passage, which was created by the perineal approach, met the prevesical space, two skin flaps from the thigh were seized by forceps introduced through the superior abdominal opening, drawn up and sutured to the depth of the newly created vault. The vagina was then packed with iodoform gauze.

Frank and Geist (22) in 1927 modified the procedure. They outlined a flap along the inner surface of the thigh. The raw edges were turned in over a tube. Two weeks later, the distal end of the tube graft was partially incised. A little later a canal was established by blunt dissection in the rectovesical septum, the distal end of the tube graft was completely separated and the graft was turned inside out with the skin inside over a vaginal plug. This graft was then sutured to the depth of the vault. Eight days later the proximal end of the original flap was completely separated from the donor area and the cut edges sutured to the vulval margin.

Grad in 1932 used several steps to swing his graft, and the mold was not used until the procedure was completed. He resorted to split-skin grafts to repair any resultant defects.

Free skin grafts. Heppner in 1872 made the first attempt to use this method, but apparently without much success. Flynn, according to Flynn and Duckett, in 1915 used free skin grafts from the external genitalia to line the vaginal tract. An excellent result was obtained after repeated dilatations. In 1930 Kirschner and Wagner used a rubber sponge prosthesis covered with Thiersch grafts. The vaginal tract was drained by a rigid rubber tube which was inserted through the sponge. In 8 to 10 days the sponge was removed and dilatations were begun. In 1938, McIndoe and Banister reported a case of the satisfactory use of a Thiersch graft over a vaginal mold which was left in place 3 to 6 months until the contractile phase of the grafting process was

over. Emphasis was placed on long-continued use of the mold. Bonney and McIndoe in 1944 were able to establish regular menses in a girl with a bicornate uterus and no cervix by joining the two halves of the uterus over a mold with a graft. Each of these authors has done the operation in about 30 cases. In 1944 Counseller and Sluder reported 35 such cases.

Simple pressure. In 1938, Frank (21) found that operation to create an artificial vagina was unnecessary in some instances. Frank's method was modified in 1940 in such a way that dilatation was accomplished by manual pressure of graduated tubes inward against the perineum one-half hour twice a day. Progress was noted in weekly office visits the first month and in semimonthly visits the second month. This, then, establishes a permanent vagina which sometimes attains a depth of 3½ inches (8.9 cm.). Steinmetz in 1940 reported a case in which this method was used. In 1941 Campbell found that he could lengthen the vagina to 3 inches (7.6 cm.) in 2 to 4 weeks by this method. He used estrin pessaries at night for the raw areas in the vagina. Dawson in 1945 got a satisfactory result in 1 case by the method of Frank in which the vagina attained a depth of 3½ inches.

Simple reconstruction. In some instances simple pressure is not sufficient for a satisfactory result; however, a very simple surgical procedure has been devised which consists simply of tunneling in the rectovesical septum, using mainly blunt dissection and then allowing the epithelial buds in the tract to proliferate and line the new vagina (Fig. 1). The vaginal canal remains patent as a result of the extended use of a vaginal mold. This method has now been used at the clinic in 14 cases. It was tried unsuccessfully as long ago as 1817 by Dupuytren who used tampons in the tract to maintain patency. In 1935, Wells gave impetus to the simple surgical procedures when he used only petrolatum gauze, which was changed every 2 days, to maintain patency in the dissected vaginal tract. Kanter in the same year used iodoform gauze for 10 days, after which a dilator was worn for a time. The results in both cases were good.

In 1938 Wharton (53) used a mold made of paraffin or balsa wood covered with a condom. One patient had been treated 10 years previously with an excellent result; the other patient would not report after 1 month. Wharton ventured the opinion that the epithelium from the lower third of the vagina (urogenital sinus) formed a large part of the epithelium of the upper two-thirds of the vagina (muellerian ducts). In 1946 Wharton (54) published reports of cases in which he used a Thiersch graft over the mold. This was done in order to hasten epithelization so as to avoid relying on the proliferative powers of the vaginal epithelial buds; also, by this procedure a decrease in the formation of scar tissue could be obtained. In that communication 16 cases were reported from Johns Hopkins. Miller, Willson, and Collins have used molds with and without Thiersch grafts and they have expressed preference for the latter method because in those cases in which it was used the vagina seemed softer, more pliable, and better epithelized. Grafts were employed in 11 of their 17 cases. Twenty-seven cases in which the dissection, no graft technique was used with good results have been reviewed by Wells, Word, Emge, and Miller and co-workers.

Miscellaneous procedures. Tissue from various sources has been relied upon to form a lining for the prepared vaginal tract with varying degrees of success. Among these are Douglas transplants of peritoneum (50), amniotic membranes (8), vernix caseosa (31), hernial sac (1), and heterogenous vaginal transplants (34).

Some surgeons do not prefer one method exclusively and use several of the previously described procedures. Sadler in 1941 reported 3 cases, in one of which the vagina was made by the husband in his attempts at coitus, in another of which only simple pressure was required to dilate the canal, and in the third of which a Thiersch graft over a mold was used. In 1945, Brady presented 4 cases; in the first case the Graves method was used, in the second a modified Graves technique was followed, in the third Wharton's technique was employed, and in the fourth only dilatation without operation was required.

ANALYSIS OF CASES

Incidence. In 1572 this condition was described by Realdus Columbus. According to

Engstadt, vaginal aplasia occurs once in 5,000 births. Owens found only 6 cases in 125,000 female hospital admissions. The incidence in our series was 1 case of congenital absence of the vagina in every 4,000 female patients.

Age. Of the 100 consecutive patients seen at the clinic with congenital absence of the vagina who underwent surgical correction, the ages varied from 14 to 49 years. Sixty-four of the patients were within the age range of 17 through 26 years, the average being 23 years for the entire series.

Family history. Ninety-six patients gave a negative family history. One patient had a sister who had amenorrhea, another had a sister with amenorrhea and infantile genitalia, still another had a sister who menstruated only twice a year, and a fourth had a sister who had congenital absence of the vagina.

Menstrual history. Ninety-nine of the patients gave a history of amenorrhea. One patient had normal menses except that the flow was through the urethra and one had vicarious menses through the lungs and rectum. Ninety of the patients became aware of their condition after they had consulted their physician because of amenorrhea. Ten patients were not disturbed by the amenorrhea but complained of inability to have intercourse. Of the 99 patients with amenorrhea, 34 complained of periodic (usually monthly) cramps in the lower part of the abdomen. These cramps were occasionally severe and were the initiating factor in causing the patient to seek medical advice.

Physical findings. Of the 100 patients with congenital absence of the vagina, 2 had infantile external genitalia and no pubic hair. In 61 patients the medical examiner was unable to palpate tubes, ovaries, or uterus, but because of the secondary sexual characteristics, it seemed that some ovarian tissue was undoubtedly present. In 10 of the 61 patients estrin levels in the urine were determined and found to be normal. In 19 patients tubes, ovaries, and uterus were palpable. In 9 patients the uterus alone was palpable. In 9 patients tubes and ovaries alone were palpable. In 2 patients ovaries alone were palpable. The psychologic attitude and emotional stability were normal in 88 of the patients, fair in 4, and poor in 8.

Abnormalities other than genitourinary. One patient had a congenitally dislocated hip and malformed foot, arm, and ribs, 1 had spina bifida occulta, 1 had a left hemivertebra, 1 had a rudimentary first rib, and 1 had a cervical spina bifida and a pelvic kidney. One patient had excessive hair on her chin, hypertension and was obese, but was not considered to have Cushing's syndrome. One patient had sacralization of the fifth lumbar vertebra.

Urologic findings. Forty-one patients underwent a urologic examination consisting of an excretory urogram and, when indicated, a retrograde pyelogram and cystoscopic examination. Twenty patients had a normal urinary tract. Twenty-one patients were found to have abnormalities of the urinary tract, of whom 7 had pelvic kidneys, 5 had solitary kidneys, 4 had a duplicated ureter or renal pelvis, 2 had pyelo-ureterectasis, 1 had a malfunctioning kidney, 1 had a solitary fused kidney, and 1 had had nephrectomy on the right for unstated reasons. Ten patients had abnormalities on the right side, and 11 patients had abnormalities on the left side.

Surgical findings. Twenty-six patients underwent pelvic operations which permitted the visualization of the pelvic organs. Of these, 4 patients had anatomically normal tubes, ovaries and uterus, 3 had hematosalpinx, 3 had endometriosis, and 10 had normal tubes and ovaries but a malformed uterus (6 infantile uteri, 2 bicornate uteri, 1 unicornate uterus, and 1 instance of cervical atresia with bilateral hematosalpinx). Five patients had normal tubes and ovaries but no uterus. One patient who had no tubes, ovaries, or uterus had vicarious menses through the lungs and rectum.

Ten additional patients underwent inguinal herniorrhaphy. In 7 of these patients, the hernial sac contained an ovary. In 1 patient the hernial sac contained a testis and in another it contained an ovotestis and epididymis (proved microscopically). The contents of one hernial sac was not stated.

Twenty-four patients had previously undergone minor vaginal plastic procedures consisting chiefly of hymenotomy. One patient had undergone a Graves procedure and another a Falls procedure for congenital absence of the vagina before coming to the clinic.

RESULTS BY MODE OF TREATMENT

McIndoe procedure. Of the 100 patients who were treated surgically for congenital absence of the vagina, 70 underwent McIndoe operations with a Thiersch graft and an inlying mold. All but 15 of the 66 patients traced had obtained excellent results. The average time which had elapsed between the operation and the follow-up for the group of 100 patients was more than 4 years. One of the patients in whom eventually excellent results were obtained required two split-skin grafts and then a tertiary graft of fetal membrane. Another patient required a regraft after the primary graft sloughed out during an attack of acute exfoliating dermatitis. Six patients had excellent results but there was some tendency to contracture if the mold was left out and they were unmarried or if the patient's husband was overseas in service and there was no intercourse. One patient who previously had undergone a Graves procedure which resulted in a rectovaginal fistula obtained an excellent result after a secondary McIndoe operation.

Ten patients obtained only satisfactory results, but usually this was because the mold was left out after 6 months, when the patients were still single, or the mold was used only occasionally between intercourse and some shrinkage occurred, and also because there was some contracture as a result of the failure of granulations to epithelize. However, 7 of this group who were married reported satisfactory sexual relations.

The results in 5 cases were unsatisfactory. In 1 instance the local physician left the mold out to treat granulations in the vault. In another case, a rectovaginal fistula developed, colostomy was done and later the rectovaginal fistula was repaired but the second attempt at correction by use of the McIndoe operation resulted in failure. One patient required a secondary Baldwin operation because the obturators were not worn long enough.

Simple reconstruction. Fourteen patients were treated by this method in which the obturator is worn after the creation of an artificial space, but grafting is not done. All have had excellent results.

In 1 of these cases Ferris reconstructed the vagina of a 15 year old girl. The patient menstruated regularly after treatment. In the 2 cases in which biopsy was performed a month or more after the operation, squamous epithelium was growing and in 1 case in which immediate biopsy was done a similar result was found.

Baldwin procedure. Fourteen patients underwent Baldwin operation in which the ileum was used to create an artificial vagina. Three patients obtained excellent results although one of these patients later needed a repair for prolapse of the bowel and another had undergone a preliminary unsatisfactory attempt at reconstruction by use of the McIndoe method. Five patients obtained satisfactory results but complained of a profuse, irritating vaginal discharge which, in 1 case, required the use of 4 or 5 sanitary napkins a day. Another patient had intestinal obstruction and a fecal fistula 2 years after the operation, and 1 reported some vaginal contracture. Four patients died in the hospital of peritonitis or intestinal obstruction. The average length of time between operation and follow-up was more than 8 years.

Other procedures. One patient underwent a Falls procedure which was apparently satisfactory but this patient could not be traced. Another patient underwent blunt dissection of the rectovesical space and the space was packed with iodoform gauze; the result was satisfactory when the patient was last heard from 8 years later.

COMMENT

Reconstruction of an artificial vagina should be attempted only in patients who are married or are contemplating marriage in the very near future or in the occasional case of hematometra, because many of the cases in which the results were unsatisfactory were single women who would not wear the obturator indefinitely and could not have marital relations because of their unmarried status. Also, if a patient is unco-operative or has a tendency to be sexually frigid, the reconstruction should not be attempted. The great majority will not require surgical removal of the uterus or its adnexa because these are usually atrophic and asymptomatic. Not infrequently these patients have an associated congenital anomaly of the urinary tract which may require surgical interference, namely, ectopic pelvic kidneys,

which may be injured during intercourse, or infected hydronephrotic kidneys lying in the pelvis. Ureterovaginal fistula may result from anomalous insertion of a ureter.

In 14 cases excellent results have been obtained without grafting. This has been possible because of the inherent ability of the newly formed artificial vagina to epithelize itself. However, if there is difficulty in controlling bleeding or in elevating the peritoneum, or if the vaginal tract cannot be opened up with ease, then a graft should be used. When grafts are not used, epithelium probably arises from the lower segment of the vagina and also from buds of epithelium arising from remnants of the muellerian ducts. Ayre took vaginal smears from an artificial vagina where no graft was used and showed the new lining to be reacting in a cyclic manner to ovarian hormones similar to the way the normal vagina reacts. Whitacre and Wang expressed the thought that the connective tissue elements in this region release a growth stimulating factor, especially after trauma. Granulations rarely form in a vagina that is not grafted but if they do they are smaller and are at the sites where bleeding occurred during the original dissection. Marshall has stated that the disadvantages of this simple reconstruction procedure are that a large, raw granulating surface is present for 2 to 3 months, that secondary hemorrhages occur not infrequently, that there is local infection, which is not serious, and that the procedure must be limited to those patients with a rudimentary vaginal pouch. We have not found these stated disadvantages to be of any consequence. The patients are usually unaware of any discomfort after a brief initial period, and there have been only occasional instances of oozing of blood from the vaginal tract. This method can be employed just as easily on the patients without a rudimentary vaginal pouch as on those with a rudimentary dimple.

Thiersch grafts produce excellent results if the take is complete and the mold is worn long enough; however, occasionally one or more areas are devoid of skin and it is usually necessary to regraft them. McIndoe pointed out that the contraction phase of a canal lined by a Thiersch graft lasts 3 to 6 months or longer and that removal of the mold before this time has elapsed will result in stricture. This principle applies also to those patients who have not had a graft, and the continuous presence of the obturator for 6 months or more is essential.

When a Thiersch graft is used over the mold as has been popularized by McIndoe, the results are usually very satisfactory but it is a more difficult procedure; we have found a greater tendency toward formation of granulation tissue, and some areas will need regrafting. This may result in more contractures than when no graft is used. Our series included 70 cases in which the McIndoe procedure was used.

The attempt at reconstruction of an artificial vagina according to the McIndoe principle should not be made if the patient is single and does not intend to be married in the near future or if she is unco-operative, because the mold must be worn for months. Most poor results are due to too early removal of the mold. The lucite mold we use is nonirritating and probably could be worn for years without any deleterious effects. Also, the mold should be worn until the perivaginal and perirectal cellulitis has subsided, the contractile phase has passed, and the entire tract has been epithelized.

When the Baldwin procedure is utilized the mortality is high (28.6 per cent in our series) and the percentage of good results is low. Many of these patients complain bitterly of the vaginal discharge. It is a more difficult operation with greater morbidity and infection. The Schubert rectal transplant method results in a mortality as high as 12 per cent. Also, there is danger of infection, there is often damage to the sphincter ani, a considerable portion of the coccyx is removed and frequently an intestinal fistula develops (27).

Operations in which pedicle grafts are used necessitate longer hospitalization and multiple stages, they are more difficult of performance than is simple reconstruction and they have a higher morbidity. Also, hair may grow on the inverted flaps. If sloughing occurs, the operation cannot be repeated easily and there is undesirable distortion and mutilation of the vulva (11).

Falls' method appears to be a simple and excellent procedure.

Simple pressure as advocated by Frank often results in a short vagina (15).

SUMMARY AND CONCLUSIONS

A simple, excellent method for creation of an artificial vagina in congenital absence has been discussed. It produces a vagina which is normal in depth, diameter, and mobility. The operation technically is very simple and consists of carefully opening the vaginal space and wearing a nonirritating mold for 6 months or longer until the contractile phase has passed. The long-continued use of the mold is of prime importance. Grafting is usually not necessary because of the marked tendency of epithelial buds in the newly dissected tract to proliferate. In our series of 14 cases in which this method was used there was no mortality and minimal morbidity, varying with the amount of pelvic cellulitis.

Reconstruction by use of intestinal transplants is not very satisfactory because of the high mortality, excessive discharge, and greater morbidity. Fourteen Baldwin operations were performed in our series.

The use of pedicle grafts is associated with higher morbidity, and necessitates longer hospitalization and multiple stage operations and, if sloughing occurs, the operation is not easily repeated.

Simple pressure sometimes results in an inadequately short vagina.

REFERENCES

1. Auvray. Quoted by Read, C. D. Irish J. M. Sc., 1944, 6: 52–57.
2. Ayre, J. E. Am. J. Obst., 1944, 48: 690–695.
3. Baldwin, J. F. Ann. Surg., 1904, 40: 398–403.
4. Idem. Quoted by Falls, F. H. (17).
5. Beck, Carl. Ann. Surg., 1900, 32: 572–574.
6. Bonney, Victor, and McIndoe, A. H. J. Obst. Gyn. Brit. Empire, 1944, 51: 24–29.
7. Brady, Leo. Ann. Surg., 1945, 121: 518–529.
8. Brindeau. Quoted by Esser, Elisabeth. J. Internat. Coll. Surgeons, 1943, 6: 496–499.
9. Campbell, Kate. Med. J. Australia, 1941, 2: 650.
10. Counseller, V. S., and Sluder, F. S., Jr. S. Clin. N. America, 1944, 24: 938–942.
11. Curtis, A. H. A Textbook of Gynecology. 5th ed., pp. 665–667. Philadelphia: W. B. Saunders Co., 1946.
12. Davis, C. H., and Cron, R. S. Am. J. Obst., 1928, 15: 196–201.
13. Dawson, J. B. N. Zealand M. J., 1945, 44: 132–133.
14. Dupuytren. Quoted by Judin, Sergey (27).
15. Emge, L. A. Am. J. Obst., 1940, 40: 917.
16. Engstadt. Quoted by Miller, N. F., Willson, J. R., and Collins, James (41).
17. Falls, F. H. Am. J. Obst., 1940, 40: 906–915.
18. Felix, W. In Keibel, Franz, and Mall, F. P. Manual of Human Embryology. Vol. 2, pp. 921–924. Philadelphia: J. B. Lippincott Co., 1912.
19. Ferris, D. O. Personal communication to the authors.
20. Flynn, C. W., and Duckett, J. W. Surg. Gyn. Obst., 1936, 62: 753–756.
21. Frank, R. T. Am. J. Obst., 1938, 35: 1053–1055.
22. Frank, R. T., and Geist, S. H. Am. J. Obst., 1927, 14: 712–718.
23. Grad, Herman. Surg. Gyn. Obst., 1932, 54: 200–206.
24. Graves, W. P. Quoted by Curtis, A. H. (11).
25. Heppner. Quoted by Marshall, H. K. (35).
26. Jewett. Quoted by Frank, R. T. J. Mount Sinai Hosp. N. York, 1941, 7: 259–262.
27. Judin, Sergey. Surg. Gyn. Obst., 1927, 44: 530–539.
28. Kanter, A. E. Am. J. Surg., 1035, 30: 314–316.
29. Kempermann, C. T. Morph. Jahrb., 1935, 75: 151–179.
30. Kirschner, M., and Wagner, G. A. Quoted by Barrows, D. N. Am. J. Obst., 1936, 31: 156–158.
31. Kleitsman. Quoted by Esser, Elisabeth. J. Internat. Coll. Surgeons, 1943, 6: 496–499.
32. Koff, A. K. Contrib. Embryol. Carnegie Institute, 1933, 24 (No. 140): 59–90.
33. McIndoe, A. H., and Banister, J. B. J. Obst. Gyn. Brit. Empire, 1938, 45: 490–494.
34. Mackenrodt. Quoted by Falls, F. H. (17).
35. Marshall, H. K. West. J. Surg., 1944, 52: 245–255.
36. Meigs, J. V. Am. J. Obst., 1938, 35: 465–466.
37. Meyer, Robert. Arch. Gyn., Berl., 1934, 158: 639–738.
38. Ibid., 1936–1937, 163: 205–308.
39. Ibid., 1937, 164: 207–357.
40. Ibid., 1937–1938, 165: 504–590.
41. Miller, N. F., Willson, J. R., and Collins, James. Am. J. Obst., 1945, 50: 735–747.
42. Mori. Quoted by Marshall, H. K. (35).
43. Nagel. Quoted by Felix, W. (18).
44. Owens, Neal. Surgery, 1942, 12: 139–150.
45. Popow. Quoted by Marshall, H. K. (35).
46. Sadler, LeRoy. J. Oklahoma M. Ass., 1941, 34: 382–385.
47. Schubert. Quoted by Judin, Sergey (27).
48. Sneguireff. Quoted by Baldwin, J. F. (3).
49. Steinmetz, E. P. West. J. Surg., 1940, 48: 169–177.
50. Stoeckel and Kroener. Quoted by Frank, R. T., and Geist, S. H. (22).
51. Vilas, Erna. Zschr. Anat. Entw., 1932–1933, 99: 599–621.
52. Wells, W. F. Am. J. Surg., 1935, 29: 253–255.
53. Wharton, L. R. Ann. Surg., 1938, 107: 842–854.
54. Idem. Am. J. Obst., 1946, 51: 866–875.
55. Whitacre, F. E., and Wang, Y. Y. Surg. Gyn. Obst., 1944, 79: 192–194.
56. Word, Buford. South. M. J., 1940, 33: 293–299.

CARCINOMA DEVELOPING IN CHRONIC DRAINING CUTANEOUS SINUSES AND FISTULAS

ALBERT K. McANALLY, M.D., and MALCOLM B. DOCKERTY, M.D., Rochester, Minnesota

ALTHOUGH the actual cause of cancer is unknown, the role of chronic irritation as an etiologic factor of importance has long commanded the attention of those interested in the subject of neoplasms. Much well deserved emphasis has been accorded the carcinogenic "tendencies" of radiodermatitis, senile keratosis, leucoplakia and so forth. The accumulated knowledge of the behavior of these lesions has often resulted in the early diagnosis of carcinoma superimposed thereupon.

The particular phase of the subject that we wish to emphasize is the occurrence of carcinoma in chronic inflammatory sinuses, for the following reasons: (1) The development of malignancy on this basis is not particularly rare. (2) The diagnosis can be made clinically at a relatively early stage. (3) The neoplasms are, in general, slow growing and can be treated successfully if diagnosed during the long latent period which usually precedes the stage of metastasis.

REVIEW OF THE LITERATURE

In 1828, Marjolin first recognized the occurrence of malignant changes in old ulcers, but it is uncertain that he described the development of carcinoma in a draining sinus. By the year 1894, Devars was able to collect from the literature reports of 39 cases. He stated that two types of lesions could be found. The first was the obvious, or overt, ulcer or tumor, and the second, a deep lesion with no trace of epithelioma at the level of the fistula. Up to the year 1931, 52 cases of malignant disease occurring in osteomyelitic sinuses had been reported and to these Benedict added reports of 12 cases from the files of the Massachusetts General Hospital, where he found an incidence of 0.5 per cent in 2,400 cases studied. In his series the average duration of the sinus prior to the malignant change was 30 years. The malignant lesion in every instance was an epithelioma. The highest incidence of malignant change occurred in sinuses involving the lower extremities and this he attributed to the poor circulation in this location and to the fact that patients were willing to neglect such foul lesions for many years. In 9 of his cases amputation of the extremity was carried out and in 2, radical excision of the growth was performed. Prognosis was favorable owing, he felt, to the fact that the neoplasms grew slowly.

Henderson and Swart concluded that if malignancy is suspected from the appearance of the sinus, foul odor, pain or hemorrhage, a biopsy should be performed. If the results of biopsy are positive, the extremity should be amputated.

Bereston and Ney, in 1941, reviewed the reports of all the cases in which metastasis had occurred from carcinoma developing in a chronic osteomyelitic sinus. They added reports of 2 cases of their own to the 7 which they had accepted from the literature. In the first case reported by Bereston and Ney, metastasis to the lungs occurred. Hellner reported, in 1936, the first case in which metastasis to the lungs occurred. In Bereston and Ney's second case there was roentgenologic evidence of bony metastasis. Two previous examples of bony metastasis had been reported by Volkmann and Krey.

In summarizing the collected reports of 7 cases, Bereston and Ney stated that only 4 were definite examples of visceral metastasis proved by autopsy. No biopsy of the enlarged lymph nodes in Volkmann's case was done and it is possible that the lesion in the femur in Krey's case was due to direct extension from the primary lesion in the tibia. In the case reported by Stewart and his associates no vis-

From The Division of Surgery, Mayo Foundation and the Section on Surgical Pathology, Mayo Clinic.

Abridgment of thesis submitted by Dr. McAnally to the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

ceral metastasis but only spread to the skin was evident. Thus, there are only 4 cases in which proved metastatic lesions definitely occurred in the viscera and only one in which cutaneous spread was noted. Bereston and Ney concluded that the rarity of metastasis may be explained by the low grade of malignancy and by the possibility that some of the reported cases may have been instances of pseudo-epitheliomatous hyperplasia rather than true malignant neoplasia.

Regarding the subject of the development of carcinoma in fistula in ano, Ewing and others had quoted Kraske as follows: "There is no satisfactory evidence that cancer develops in tissues altered by hemorrhoids, fistulae or cicatrices." Since this statement was made, there has been much discussion pro and con. Pennington pointed out in 1923, that fistulas had been known to exist for 35 to 46 years without the occurrence of malignant changes. However, he remarked that epitheliomas occasionally are found a short distance up the rectum where they are supposed to arise from old fistulous openings and similar foci of chronic disease.

Lockhart-Mummery and Dukes agreed that occasionally carcinoma occurs in fistulous tracts and reported 2 cases in which carcinoma arose in the primary opening of a chronic fistula in ano.

Rosser, in 1931, reported 7 cases in which carcinoma developed in anal fistulas. One patient had been operated on for a fistula and an adjacent polyp 1 year before and the latter lesion recurred. Another patient had small, warty growths of squamous-cell epithelioma at the external opening. In the 5 other cases, adenocarcinomatous tissue was found invading the fistulous tracts, apparently originating at the primary opening but without tumor formation at this point, except in 1 case.

In 1945, David stated that he had seen 5 instances in which carcinoma developed in long-standing fistulous tracts around the rectum. In 1 case the lesion was a basal-cell carcinoma and in the others it was an epithelioma, neither of which is a type that corresponds to what usually is seen in malignant disease of the rectum. The fistulas in 3 of these cases developed in long-standing lesions of lymphogranuloma inguinale involving the rectum.

A rather extensive review of the literature reveals little information on the subject of the occurrence of epitheliomatous changes in chronic empyemic sinuses. Sauerbrach and O'Shaughnesy did not even make any reference to the occurrence of malignant changes in a chronic sinus when they discussed the complications of chronic empyema. Only one reference was found in the literature and this was simply a case report by Schmid, who concluded that carcinomatous changes in fistulas, in general, form rare complications in chronic, purulent processes. In his particular case, pneumonia with effusion developed in 1916, and this was treated by thoracotomy; malignant changes were noted in the persistent sinus in 1935, and the patient died within several months, in spite of the use of roentgen and radium therapy.

MATERIALS AND METHODS

This is a review of all those cases encountered at the Mayo Clinic in which malignant changes had taken place in chronic, cutaneous sinuses and fistulas, particular emphasis being placed on cases of chronic osteomyelitic sinuses in which malignant changes occurred and in which metastasis was a complicating factor. Nine such cases are reported, along with 3 cases of fistula in ano and 1 case of empyemic sinus from the pleural space.

Blocks of tissue were obtained from the new growths, the infected bone and the adjacent lymph nodes when they were available. These blocks were placed in bottles of 10 per cent solution of formalin. The soft parts were sectioned by the freezing method and were stained with hematoxylin and eosin. The blocks of bone were first decalcified with 5 per cent solution of nitric acid. The stained sections were examined microscopically in order to determine the grade of malignancy, and malignant tissue occurring in chronic osteomyelitic sinuses was examined carefully to rule out the possibility of pseudo-epitheliomatous hyperplasia. The nodes were examined for evidence of metastasis, and the sections made of the "inflammatory" bone were examined for evidence of tuberculosis.

CLINICAL FEATURES

The files of the Mayo Clinic were productive of 9 cases in which malignant changes occurred in osteomyelitic sinuses (0.23 per cent of approximately 4,000 cases), and 3 in which fistula in ano underwent this change (0.1 per cent of 3,000 cases). In addition, 1 empyemic sinus was the site of a similar complication (0.07 per cent of 1,500 cases). These 13 cases serve as the basis for the present study. There were 11 men and 2 women. The duration of the inflammatory tract was 48 years as a maximum and 2 years as a minimum, with an average of 26.7 years. The lesion was located in the tibia in 6 cases and in the femur, shoulder, hand and pleural space in 1 case each. Three lesions were fistula in ano.

Signs and symptoms. Osteomyelitic group.—The presence of a new growth was obvious in the sinus in 7 of the 9 cases, and 6 patients had observed a recent increase in foul-smelling discharge. In 1 case some bloody drainage developed. In only 3 cases was pain a prominent symptom. Enlarged regional lymph nodes were present at examination in 7 of 9 cases and the nodes became invaded later in 2 instances. There was no evidence of tuberculous involvement of the bone. The serologic reaction for syphilis was positive in 1 case. Roentgenograms were interpreted as revealing chronic osteomyelitis and in 1 case the following notation was added: "There is irregular destruction of bone which could be secondary to contiguous malignancy." A pathologic fracture was noticed in 2 instances.

Fistula in ano group.—The chief complaint was persistent drainage; in 1 case the discharge was hemorrhagic and in 1 there was a foul odor. Proctoscopic examination revealed no primary neoplasm in the rectum. In 2 cases an indurated area had been noted 4 and 7 months, respectively, previously in the tract. Bacteriologic studies in 1 case revealed neither tubercle bacilli nor Actinomyces. Flocculation tests gave negative results. The sedimentation rate in 1 case was 59 millimeters in 1 hour (Westergren method). In 1 case, two biopsies of deep-lying tissue were necessary before malignant tissue was noted, which illustrates the fact that misleading information may be obtained from superficial examination.

Empyemic group.—There was only 1 case in this group. Twenty-three years previously, the patient with empyema underwent resection of the ribs for pleural effusion, and foul drainage persisted. Three years before admission dull, steady pain had been noticed. Three months prior to admission, blood had appeared in the discharge and dyspnea on exertion had developed. Examination of the sputum and of the discharge from the sinus had failed to reveal tubercle bacilli or sulfur granules. The sedimentation rate was 83 millimeters, the leucocyte count was 8,500 per cubic millimeter of blood, the erythrocyte count was 4,200,000 per cubic millimeter and the hemoglobin measured 14 grams per 100 cubic centimeters of blood. Roentgenograms of the thorax had revealed only "thickened pleura."

PATHOLOGIC FEATURES

Osteomyelitic group.—In 2 of the 9 cases (22.2 per cent) metastasis to the regional lymph nodes occurred as a complication.

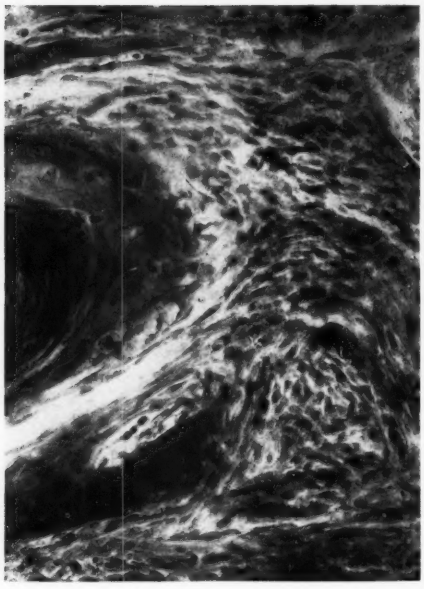
In all of the 5 sections of bone available for study, evidence of nonspecific inflammation was found.

All the lesions were characteristic of squamous cell epithelioma and, for the most part, were of a low grade (Broders' method); 3 were graded 1, 5 were graded 2, and 1 was graded 3. Of the 2 lesions which metastasized, 1 was graded 2 and the other was graded 3.

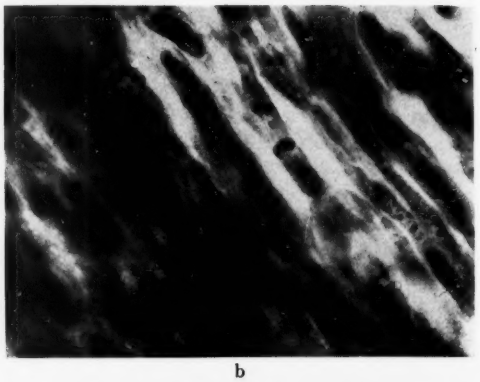
One lesion was originally reported as a grade 3 epithelioma and fibrosarcoma, but a review of other sections revealed that it was actually an epithelioma simulating a fibrosarcoma (Fig. 1). This is not a new concept because it has been observed in so called sarcoma of the thyroid and in oat cell tumor of the lung.

In 1 case the biopsy was reported as revealing epithelial hyperplasia and the lesion was excised locally but in less than a year it had recurred and specimens from the amputated leg were characteristic of grade 1 epithelioma.

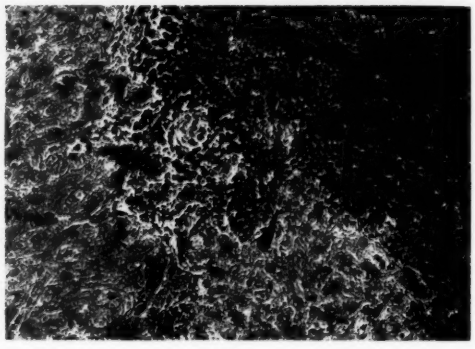
CASE 1. A 57 year old man had had a draining sinus in the upper third of the right tibia for 48 years, and 1 year before admission he had noted a small nodule at the side of the tract. Only a biopsy was done, which revealed much keratin and some epithelial pearls. In addition there were pale cells with hyperchromatic nuclei, and mitotic figures were



a



b



c

Fig. 1. Grade 3 squamous cell epithelioma simulating fibrosarcoma. This lesion occurred in a chronic osteomyelitic focus in the right foot. a, ×195. b, Note mitotic figures (×590). c, Metastatic lesion in inguinal lymph node (×135).

quite rare. The lesion was interpreted as a low grade 2 squamous cell epithelioma but the patient left without undergoing further surgical procedures.

CASE 2. A 61 year old man had had a chronic draining sinus in the right medial malleolus resulting from osteomyelitis at the age of 14 years. For a year before admission there had been increased swelling and pain. A cauliflower-like mass measuring 10 by 7 by 1.6 centimeters was present. Microscopically, epithelial hyperplasia was present and there were occasional mitotic figures which were definitely some distance superficial to the basement membrane. Both epithelial pearls and intercellular bridges were present. Many plasma cells and fibroblasts were observed. The lesion was classified as a grade 1 epithelioma.

CASE 3. A 50 year old man had had a draining sinus in the lower part of the right leg for 10 years. Four months before admission he had observed some "little growths" at the site of ulceration, and on examination at the clinic a cauliflower-like growth measuring 11 by 8 by 0.5 centimeters was noted. Microscopically, no pearls were seen but there were cords and clumps of pale-staining squamous cells that penetrated irregularly into the surrounding tissue. Nuclei were hyperchromatic and of variable size. The lesion was classified as a grade 2 epithelioma.

CASE 4. A 45 year old man had had the first symptoms of osteomyelitis of the lower part of the right femur at the age of 8 years. At age 15 there were pain and swelling in the right hip and pus was aspirated; since then there had been continuous purulent drainage. On examination a mass around the ostium of the sinus at the upper posterior aspect of the right thigh measuring 6 by 5 by 2 centimeters was observed. Microscopically, the squamous epithelial cells were large, and hyperchromatic nuclei and occasional mitotic figures were seen. Only minimal pearl formation was noted. Many polymorphonuclear leucocytes, fibroblasts, erythrocytes, and plasma cells were present. The lesion was graded 2.

CASE 5. A 57 year old man had had a draining sinus in the right leg for 33 years. Four years before the first admission a sequestrum had been excised. In October, 1941, examination revealed a granulating mass 3 by 3 centimeters and biopsy of superficial tissue disclosed what was reported as epithelial hyperplasia; however, the excised specimen removed at operation contained numerous epithelial pearls

and some pearls were observed in a nearby lymph follicle. Occasional mitotic figures were seen. On July 24, 1942, an amputation was performed at the juncture of the lower and middle thirds of the right femur. The papillomatous lesion extended 1.5 centimeters above the surface of the skin; it was 10 centimeters long by 2 centimeters wide. Microscopically, numerous cords and strands of squamous cells in which there were occasional mitotic figures were observed. Pearls were numerous, and often there was peripheral palisading of the epithelial cells. The lesion appeared to be a grade 1 epidermoid carcinoma.

This case illustrates the misleading information which may be obtained from a biopsy of superficial tissue.

The following case is of interest because carcinoma of the sinus was complicated by the occurrence of metastasis.

CASE 6. In 1917 the patient had received an extensive crushing and burn injury to the right hand. Since then the skin had broken down and had healed on numerous occasions. In March, 1938, the hand was explored and a keloid was excised from the dorsum. In November, 1938, roentgenograms revealed osteomyelitis of the metacarpals of the right hand and at that time some sequestra were removed. Since then there had been constant drainage. When the patient was first seen at the clinic in March, 1939, examination of the dorsum of the right hand revealed an ulcer 3 inches (7.6 cm.) in circumference with dirty necrotic bone in its base. At that time the third, fourth, and fifth fingers and the corresponding metacarpals were amputated. Microscopically, pearls were present as were pale cells with pathologic mitotic figures. Some of the cells contained vacuoles which gave them a pagetoid appearance. There was invasion of bone, and many polymorphonuclear leucocytes, giant cells, plasma cells, and mast cells were seen. This lesion was classified as a grade 2 epithelioma. The patient was admitted for the second time on April 22, 1942, because of considerable pain in the right axilla. Physical examination revealed a mass the size of an egg in the axilla and this was incompletely excised because of the extensive invasion. Microscopically the regional lymph nodes showed polygonal cells with pale cytoplasm and large, hyperchromatic nuclei (Fig. 2). Very few mitotic figures were seen and fibrous tissue had replaced most of the lymphoid elements. The lesion was interpreted as a grade 2 epithelioma.

CASE 7. A 58 year old woman had had drainage, off and on, from a sinus located at the lower third of the right tibia for 48 years. Three months before admission a "painless knot" began to grow above the right ankle. On examination, the right leg exhibited a healed, scarred sinus on the middle of the anterior surface. Over the anterior surface of the lower third there was a cauliflower-like mass measuring 7 by 5 by 2.5 centimeters. Microscopically, there were

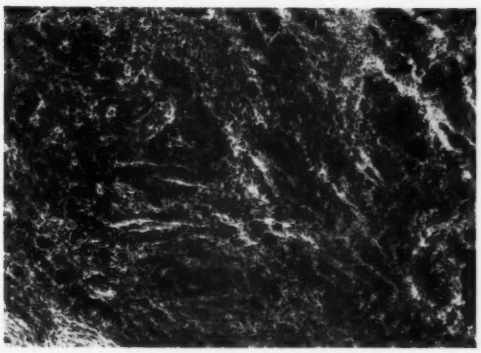
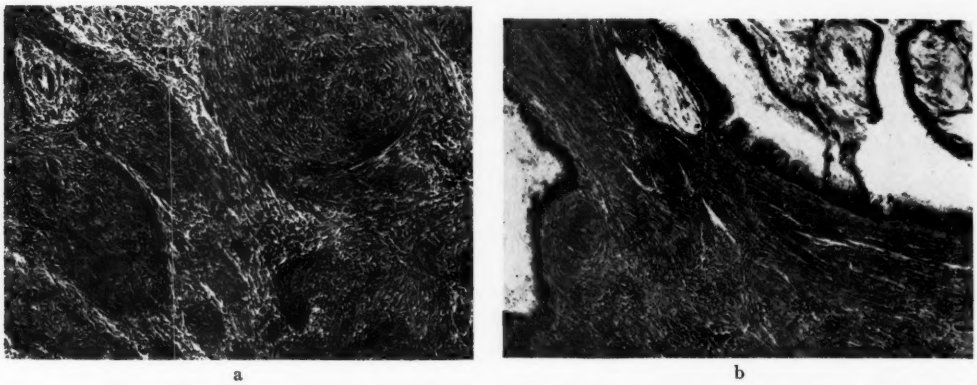


Fig. 2. Axillary lymph node metastasis showing grade 2 squamous cell epithelioma. Primary was grade 2 squamous cell epithelioma developing in chronic osteomyelitis of the right hand (×90).

huge epithelial pearls—many containing cells with intercellular bridges. Peripheral palisading was prominent and, in addition, there were cords, plugs, and strands of epithelial cells. The lesion was considered to be a grade 1 squamous cell epithelioma.

CASE 8. A 47 year old man had undergone a left glenohumeral disarticulation at the age of 17 years after his arm had been caught in a machine. Three years before admission the scar over the amputation site had broken down, discharging clear serum that gradually became purulent and foul-smelling. For 7 months a reddish growth measuring 6 by 4 by 1 centimeter had been noted. Excision of the growth, the remaining portion of the scapula and a portion of clavicle was carried out. Microscopically, mitotic figures were noted in the pale epithelial cells which were arranged in typical pearl formation. The lesion was interpreted as a grade 2 epithelioma.

CASE 9. A 37 year old man had had osteomyelitis with drainage for 23 years. On April 10, 1933, when he reported to the clinic, he stated that since the last visit in 1927, the painful leg had improved but the sinus continued to drain. Two months before admission soreness developed in the ankle and 10 days before, hemorrhage occurred from the sinus. On August 22, 1933, the right leg was amputated at the juncture of middle and upper thirds. Four months later an inguinal lymph node was excised. The specimen consisted of the right foot, the lower two thirds of the leg and an excised lymph node. A sinus was located just superior to the medial malleolus and this led down into the marrow of the tibia where there was a cavity which measured 7 by 6 centimeters and the wall of which consisted of firm rubbery tissue 3 centimeters in thickness. Certain sections showed many large squamous cells with hyperchromatic nuclei and numerous mitotic figures, and an occasional well developed epithelial pearl was seen (Fig. 1a). Other sections showed large spindle cells with pale cytoplasm and pathologic mitotic figures (Fig. 1b). Many polymorphonuclear leucocytes and



a b

Fig. 3. Malignant changes occurring in chronic fistula in ano. a, Section showing grade 1 squamous cell epithelioma (×110). b, Section showing grade 1 mucous adenocarcinoma (×55).

plasma cells and an occasional foreign body giant cell were noted. Microscopic section of the lymph node showed numerous large, pale epithelial cells with hyperchromatic nuclei. Mitotic figures were numerous (Fig. 1c).

Both the primary and metastatic lesions were interpreted as grade 3 squamous cell epitheliomas simulating fibrosarcoma.

Fistula in ano group.—Of the malignant lesions developing in a fistula, 1 was a squamous cell epithelioma and 2 were adenocarcinomas. All 3 were grade 1 lesions. No sinus was identified and the rectal mucosa was normal in each case.

CASE 10. A 49 year old man had had a persistent draining fistula for 22 years. The anal canal and mucosa appeared normal. Examination of the tissue obtained by curettement revealed cords and strands of squamous malignant cells with no pearls (Fig. 3a). Plasma cells and polymorphonuclear leucocytes were numerous. Apocrine glands were noted in the deep tissues. This was classified as a grade 1 squamous cell epithelioma.

CASE 11. Eighteen years before the patient was admitted at the clinic an ischioanal abscess was incised and it continued to drain until 4 years before admission when the fistula healed, but occasionally a small amount of pus appeared from the rectum. Four months before admission pain was noted and a tumor appeared. Microscopic examination of tissue obtained when the right ischiorectal fossa was laid bare showed definite acinar formation, and there were well differentiated columnar epithelial cells. Plasma cells were numerous but no mucin was visible. The lesion was a grade 1 adenocarcinoma.

CASE 12. A 58 year old man had had a fistula for 16 years with persistent drainage, and 6 months before admission a honeycomb region of draining sinuses had appeared. The site of tumefaction measured 6 by 8 centimeters. The growths plus the distal 4 or 5 inches (10 or 12 cm.) of the rectum were excised. Microscopic examination of the tissue disclosed well formed acini containing much mucin, and the lesion was considered to be a grade 1 adenocarcinoma (Fig. 3b). The lymph nodes were the site of inflammatory changes.

Empyemic group.—There was only 1 case in this group.

CASE 13. A 55 year old man was seen in February, 1946, on account of a chronic empyemic sinus which had been draining since 1918, and had followed thoracotomy for a pleural effusion. Three months before admission, blood began to appear in the foul smelling discharge. Microscopic examination of the excised tract and thickened pleura disclosed much hemorrhage and many lymphocytes and there were numerous cords and plugs of epithelial cells. Pearls and intercellular bridges were present and there was a tendency toward peripheral palisading. Occasional mitotic figures were seen. The lesion was a grade 2 epithelioma (Fig. 4).

TREATMENT AND RESULTS

Osteomyelitic group. Three patients were treated by amputation and 1 of these had postoperative therapy with roentgen rays. One of these 3 patients lived 11 years and died from gastric carcinoma, another was alive 21 years postoperatively and the third died from chronic nephritis 14 years after amputation.

One patient underwent partial amputation in March, 1939, and in April, 1942, metastatic lesions were observed in the axillary nodes. Death occurred in July, 1942.

One patient underwent excision and cautery in September, 1921, and died in July, 1922. The cause of death was not stated. Radium therapy was apparently without benefit.

Another patient underwent excision of soft tissue and bone from the site of a disarticulation of the left humerus that had been performed 40 years earlier. The patient was given roentgen therapy and 4 years later had had no recurrence.

Two patients underwent excision and curettement one or more times and eventually required amputation. They are both well 4 and 13 years, respectively, after amputation.

In 1 case (Case 1) in which only a biopsy was done, operation was not performed at the clinic. However, a letter was sent immediately to the patient's family physician advising that the extremity be amputated because of the malignant nature of the lesion. We have been unable to trace this patient.

Fistula in ano group. In Case 10, the cavity of the anal fistulous tract was simply curetted and then packed with iodoform gauze. This was done on February 15, 1922, and on October 21, 1923, the patient died of carcinomatosis.

In Case 11, the entire right ischiorectal fossa was laid bare, and the right wall of the rectum was exposed for about 3 inches (7.5 cm.). Between March 12 and March 20, 1931, 2,343 milligram hours of radium were applied to the region of the sinus, and from March 14 through March 18, 1931, 4,200 milligram hours of radium were given to the left groin and 4,186 milligram hours administered to the right groin. From June 12 to June 13, 1931, 4,200 milligram hours were applied again to the right groin. At biopsy on September 11, 1931, tissue from the right ischiorectal fossa proved to be malignant. Consequently, treatment of the lesion with radon needles was carried out as follows: September 12, 1931, 480 milligram hours; December 11, 1931, 782 milligram hours; and March 24, 1932, 336 milligram hours. The patient died on April 12, 1941, from "carcinoma of the rectum" according to his family physician.

In Case 12, left loop colostomy was performed after biopsy of deep tissues revealed colloid adenocarcinoma, grade 1, on October 12, 1943. At that time no involvement of the lymph nodes was observed. On November 2, 1943, diathermy was used to remove all the perirectal skin over the growth and the growth itself plus the distal 4 to 5 inches (10 to 12 cm.) of the rectum. The patient had received 8 weekly roentgen ray treatments elsewhere preoperatively, but the amount was not stated. Postoperatively no more radiation was given. Correspondence on July 15, 1946, indicated that the patient was living and well and had had no recurrence.

Fig. 4. Grade 2 squamous cell epithelioma occurring in a chronic empyemic sinus (×65).

Empyemic group. The malignant empyemic sinus was treated by radical excision after the removal of two ribs. However, it was felt that not all of the neoplastic tissue was excised. When the patient left the hospital 2 weeks after operation, he was complaining bitterly of pleural pain and required frequent doses of opiates. He was not heard from subsequently.

COMMENT AND SUMMARY

It has been thought that Cohnheim's theory of chronic irritation accounted for the malignant change occurring in these tracts. However, we feel that too much emphasis has been

placed on the factor of chronic irritation, and the basis for our attitude is the occurrence of a low incidence of malignant change in our series—0.23 per cent in the cases of osteomyelitis, 0.1 per cent in the cases of fistula in ano, and 0.07 per cent in the cases of chronic empyema. Milgram observed a patient with osteomyelitis for 62 years without finding any evidence of neoplastic change, and Pennington reported that DePage had occasion to treat a benign fistula in ano that had existed for 38 years. Rokitansky examined the third specimen of squamous cell epithelioma developing in an osteomyelitic tract (Dittrich's case) and observed that epithelial cells were growing down the sinus deep into the cavity of the bone. Cone, Schindler, Kaufmann and Brunschwig agreed that there is not much dispute that epitheliomas form from preformed epithelium and that a fistula from a diseased bone, which has become epithelized, may undergo malignant change.

White and Weidman stated that mitotic figures are seen in simple inflammation and regeneration, and that the diagnosis of carcinoma in chronic ulcers is unjustifiable, except when infiltration extends to the level of the sweat glands, or farther. Consequently, they stated that many of the so called carcinomas that develop in a sinus of chronic osteomyelitis are not really malignant but are examples of pseudoepitheliomatous hyperplasia and consequently the incidence of metastasis in such cases is low. However, Broders concluded that the day has passed when epithelium can be considered noncancerous, or, at most, only precancerous because it is within the confines of the basement membrane; and, conversely, it is not carcinomatous simply because it has penetrated the basement membrane. The character of the individual cell is the important factor.

Again it must be emphasized that the two conditions, namely, hyperplasia and neoplasia, may coexist. The biopsy in Case 5 revealed epithelial hyperplasia but examination of blocks from the excised specimen revealed epithelial pearls with occasional mitotic figures. Nine months later the sinus had persisted and another irregular, raised tumor measuring 10 by 2 by 1.5 centimeters, had appeared, sections of which showed cords and strands of squamous cells with occasional mitotic figures. The presence of pearls and intercellular bridges was noted and, in addition, there was a tendency to peripheral palisading. At that time amputation of the patient's right leg was carried out. Also in Case 12 the first biopsy was reported as disclosing epithelial hyperplasia with keratosis, but microscopic examination of sections from the excised specimen revealed well formed acini with much mucus, and the lesion was diagnosed grade 1 adenocarcinoma. It is granted that epithelial hyperplasia occurring in a chronic osteomyelitic sinus may be misinterpreted as a manifestation of epithelioma, with the result that a needless amputation may be performed. However, we think that when the biopsy of tissue from a chronic draining sinus or fistula discloses epithelial hyperplasia, a wider excision of the sinus should be performed and blocks should be studied carefully for evidence of malignant changes.

Hellner, Benedict, and Niebauer pointed out the roentgenologic findings which would make one suspect that malignant changes are taking place around osteomyelitic cavities. This change consists of areas of rarefaction observed in the bone surrounding the cavities. Such a change occurred in our Case 9 (Fig. 5).

Devars, in his review, stated that of the 39 cases of osteomyelitis in which malignant changes occurred, metastasis to the lymph nodes was noted in 50 per cent and the prognosis was especially grave. No photomicrographs were presented as evidence of metastasis. In the 12 cases reported by Benedict, no metastasis was observed, and he concluded that the prognosis was favorable owing to the fact that the neoplasm grew slowly and usually was of a low order of malignancy. Up to the year 1941, there were only 7 cases of epithelioma occurring in an osteomyelitic sinus in which proved metastasis occurred, and Bereston and Ney added 2 more cases to the literature. In our series of 9 cases of osteomyelitis in which carcinoma developed metastasis occurred in 2 cases (22.2 per cent). One of these patients was living 13 years after amputation of a leg.

In 6 of our 9 cases (66.7 per cent) there were enlarged lymph nodes at the time of operation.

In none of these was biopsy performed but 1 patient died a year later. Two of the 3 patients without palpable nodes eventually had metastasis to the nodes, proved by biopsy. Accordingly, we propose that even in the face of negative results on biopsy, roentgen ray treatment should be given over the regional nodes, and even a prophylactic dissection of these nodes might be considered.

The neoplasms which occur in chronic fistula in ano may be of a squamous cell or basal cell type or glandular in structure. Usually those arising near the anus are adenocarcinomas, but owing to the presence of both squamous and columnar epithelium at the dentate line, the growth may be of an epitheliomatous nature also. This view is strongly advocated by Rosser (23). Hermann, as well as Tucker and Hellwig, have demonstrated well developed tubular structures which run from the crypts of Morgagni into the submucosa and sometimes into the internal sphincter. In 1945, Kratzer stated that these ducts could provide a pathway for infecting organisms to penetrate the muscle surrounding the anal canal and thus could produce abscesses with subsequent fistulas.

We examined 5 normal anal rings from specimens removed in combined abdominoperineal resection and demonstrated the presence of erratic glands in the depths of the crypts. We agree with Kratzer that when there is cryptitis, these glands may provide a pathway for infecting organisms to penetrate the sphincter, as a result of which an ischioanal abscess and subsequent fistula may develop. Also, we agree with Rosser (23) that malignant changes may occur in either of the two types of epithelium present, as adenocarcinoma occurred in 2, squamous cell epithelioma in 1 of our cases.

The epithelium which became malignant in our case of chronic empyema probably was derived from an inward growth of the surface epithelium, just as the surface epithelium grows down to line the chronic osteomyelitic sinus. Since there is no good reason to support the idea that the pleural endothelium may undergo metaplasia, we subscribe to the theory that epithelium came from epithelium in this case because at operation the old sinus was observed to be completely epithelized.

Fig. 5. Grade 3 squamous cell epithelioma invading an osteomyelitic cavity. This demonstrates the small areas of rarefaction in sclerotic bone surrounding the cavities which Hellner said suggest malignant invasion.

CONCLUSIONS

1. Malignant changes in a chronic osteomyelitic sinus should be suspected when a growth appears in the sinus, the discharge becomes more foul-smelling or hemorrhagic, a painful swelling appears and when the roentgenogram reveals a pathologic fracture or areas of rarefaction surrounding the osteomyelitic cavity. There were 9 such cases in our series.

2. In our series there were 2 cases in which metastasis occurred from a malignant lesion in a chronic osteomyelitic sinus; these added to the 9 cases reported in the literature make 11 cases in which distant spread occurred.

3. It is proposed that the regional lymph nodes be treated with roentgen rays and that even a prophylactic dissection of these nodes be considered.

4. The transitional epithelium from the erratic glands of the anal crypts probably in-

vades the fistula in ano tracts, and this may account for the fact that acini are located in some of the fistulous tracts which have shown malignant change. Three such cases are presented in our series.

5. Malignant disease occurring in a chronic empyemic sinus is a surgical rarity. There was 1 case in our series.

6. When the biopsy reveals epithelial hyperplasia, the sinus or fistula should be excised and blocks studied for evidence of malignant changes. If neoplastic tissue is found, amputation should be done in cases of osteomyelitis and rather radical excision should be done for fistula in ano and empyemic sinuses.

REFERENCES

1. Benedict, E. B. Surg. Gyn. Obst., 1931, 53: 1-11.
2. Bereston, E. S., and Ney, Charles. Arch. Surg., 1941, 43: 257-268.
3. Broders, A. C. J.Am.M.Ass., 1932, 99: 1670-1674.
4. Brunschwig, Alexander. Radiology, 1935, 24: 627-630.
5. Cohnheim. Quoted by Bereston, E. S., and Ney, Charles.
6. Cone, S. M. Bull. Johns Hopkins Hosp., 1897, 8: 146-151.
7. David, V. C. Surgery of the Rectum and Anus. In Lewis, Dean, and Walters, Waltman, Practice of Surgery. Chap. 6, p. 86. Hagerstown, Maryland: W. F. Prior Co., Inc., 1945.
8. Devars, M. Lyon méd., 1894, 76: 510-514.
9. Dittrich. Quoted by Benedict, E. B.
10. Ewing, James. Neoplastic Diseases; a Treatise on Tumors. 3rd ed., p. 710. Philadelphia: W. B. Saunders Co., 1928.
11. Hellner, H. Quoted by Bereston, E. S., and Ney, Charles.
12. Henderson, M. S., and Swart, H. A. J. Bone Surg., 1936, n.s. 18: 56-60.
13. Hermann, Gustav. Quoted by Pennington, J. R.
14. Kaufmann, E. Quoted by Blanco, Pio. Am. J. Cancer, 1933, 19: 373-378.
15. Kratzer, G. L. Histopathology of the Anal Ducts. Thesis, Graduate School of the University of Minnesota, 1945.
16. Krey, W. Quoted by Bereston, E. S., and Ney, Charles.
17. Lockhart-Mummery, J. P., and Dukes, Cuthbert. Surg. Gyn. Obst., 1928, 46: 591-596.
18. Marjolin. Quoted by Benedict, E. B.
19. Milgram, J. E. J. Bone Surg., 1931, n.s. 13: 319-324.
20. Niebauer, J. J. J. Bone Surg., 1946, n.s. 28: 280-285.
21. Pennington, J. R. A Treatise on Diseases and Injuries of the Rectum, Anus and Pelvic Colon. p. 323. Philadelphia: P. Blakiston's Son & Co., 1923.
22. Rosser, Curtice. Am. J. Surg., 1931, 11: 328-333.
23. Rosser, C. Tr. Am. Proct. Soc., 1934, 35: 65-71.
24. Sauerbrach, Ferdinand, and O'Shaughnesy, Laurence. Thoracic Surgery. Pp. 74-75. Baltimore: William Wood & Co., 1937.
25. Schindler, J. Quoted by Cone, S. M.
26. Schmid, R. Čas. lék. česk., 1936, 75: 559-562.
27. Stewart, C. D., Obermayer, M. E., and Woolhandler, Harry. Arch. Derm. Syph., Chic., 1940, 41: 545-550.
28. Tucker, C. C., and Hellwig, C. A. Surg. Gyn. Obst., 1934, 58: 145-149.
29. Volkmann, R. Quoted by Bereston, E. S., and Ney, Charles.
30. White, Cleveland, and Weidman, F. D. J. Am. M. Ass., 1927, 88: 1959-1963.

THE EFFECT OF INTRAVENOUS GLUCOSE AND AMINO ACIDS ON GLYCOSURIA AND URINARY OUTPUT IN HUMANS

CHARLES E. LOCKHART, M.D., Columbia, Missouri, and ROBERT ELMAN, M.D., F.A.C.S., St. Louis, Missouri

THE proper rate at which intravenous solutions of glucose should be injected without producing glycosuria and an unwanted diuresis is of obvious clinical importance. This was studied in normal adult individuals given single 1 liter intravenous injections of various glucose solutions under standard conditions but at varying controlled rates. The findings reveal that a slower rate of administration than is ordinarily used should be employed if these undesirable factors are to be eliminated. In addition, the experiments indicate that amino acids, either as such or as hydrolyzed protein, when given in combination with glucose solutions, tend to increase the rate of utilization of glucose. This effect was evidenced by the lessened degrees of glycosuria and the lower blood sugar curves which were observed when glucose was administered simultaneously with amino acid solutions than when glucose alone was given at the same rates.

Since 1900, various workers have sought to determine the rate of utilization of glucose in humans and experimental animals, in both normal and abnormal states. It has long been recognized that an accurate glucose "tolerance" can be determined only by introducing the glucose directly into the blood stream, thereby eliminating the variable factors of absorption from the alimentary tract. In 1905 Blumenthal first studied the utilization of glucose by the tissues after intravenous injection. Using normal rabbits, he injected varying single doses at 15 minute intervals and observed a retention between 0.15 and 0.32 gram glucose per kilogram body weight every 15 minutes (0.6 to 1.2 gm. per kgm. per hour) without glycosuria. Using the same intermittent injection methods, Comessati in 1906 demonstrated that the rate of utilization was slightly increased in rabbits during and after exercise.

Continuous intravenous injection was first introduced by Woodyatt, Sansum, and Wilder in 1915, in order to arrive at more accurate figures than could be obtained by the intermittent method. They administered solutions of 18 per cent glucose to normal dogs, rabbits, and adult humans (4 laboratory workers) continuously over periods up to 4 hours in humans, 12 hours in dogs, using a motor-driven pump to aid in regulating different injection rates. On the basis of their observations, they stated that glycosuria consistently appeared at injection rates above 0.9 gram glucose per kilogram body weight per hour, and did not appear at rates below 0.8 gram per kilogram per hour. No species or sex differences were observed. On the basis of this report, the figure 0.85 gram per kilogram per hour has been looked upon as being the normal rate of utilization of glucose during intravenous injection in humans and has remained without further experimental verification for 32 years. Sansum and Wilder reported observations in 1917 on glucose utilization in abnormal states. They stated that glucose tolerance was decreased in patients with hyperthyroidism, chronic pancreatitis, mild diabetes, acromegaly, and diabetes insipidus. No lowering of tolerance was seen in patients with alcoholic cirrhosis of the liver.

Postoperative utilization of intravenous glucose was studied by Fantus in 1936. In a series of patients receiving over 200 grams of glucose per day, glycosuria was observed in

From the Department of Surgery, Washington University, School of Medicine, and Barnes Hospital, St. Louis, and The Ellis Fischel State Cancer Hospital, Columbia, Missouri.

Presented in the Forum on Fundamental Surgical Problems before the Clinical Congress of the American College of Surgeons, New York, September 8 to 12, 1947.

Aided by a grant from the Commonwealth Fund.

TABLE I.—EFFECT OF AMINO ACIDS ON GLYCOSURIA FOLLOWING INTRAVENOUS GLUCOSE

Solution	Rate of injection	No. injections	No. patients showing glycosuria
Glucose alone	Less than 0.5 gm./kgm./hr.	6	1
Glucose and amino acids		6	0
Glucose alone	More than 0.5 gm./kgm./hr.	68	68*
Glucose and amino acids		24	19†

*Range of glycosuria, 2 to 6 grams
†Range of glycosuria, trace to 38 grams

over half of the subjects. The rate of injection of the glucose solutions, however, was not regulated. In 1938, Winslow reported another study of glycosuria in postoperative patients who were given intravenous glucose at various controlled rates. This author found a greater tendency for glycosuria to appear during the first 5 days after operation than at any other time and at slower rates of administration than had been observed by Woodyatt in normal animals and humans. For example, when 10 per cent glucose was injected at rates of .4 to .8 gram per kilogram per hour during these postoperative days, glycosuria would appear in amounts up to 5 per cent of the glucose given. When 5 per cent glucose was used, glycosuria was seen to occur in rates as low as 0.35 gram per kilogram per hour; however, even when a total of 150 grams was administered at this rate usually less than 2.5 grams would be lost through glycosuria.

MATERIALS AND METHODS

One hundred and four timed and controlled 1 liter injections of glucose solutions were given intravenously to 32 selected adult humans. These subjects were patients in the general surgical wards of the two hospitals; they were considered normal in that all were either awaiting plastic or other elective procedures, and consented to postpone their day of operation in order to take part in this study, or they had had their operation at least 8 to 10 days previously and were ambulatory and about to be discharged from the hospital. All subjects exhibited normal urinalyses, normal blood glucose, and nonprotein nitrogen levels, and were in a normal state of nutrition on regular diets. Their average weight was 69 kilograms. Each subject was weighed the evening before the experiment and the rate of administration of glucose was calculated upon this basis. The glucose solutions employed were those commonly used in hospital wards, and were administered intravenously in the usual amount (1 liter) at various rates, ranging from 0.35 to 3.1 grams per kilogram per hour. The presence and degree of glycosuria resulting from each injection and the degree of associated diuresis were measured in each case. The following solutions were utilized: (1) 5 per cent glucose in water; (2) 5 per cent glucose in isotonic saline; (3) 10 per cent glucose in water; (4) 10 per cent glucose in isotonic saline; (5) 5 per cent amigen in 5 per cent glucose; (6) 5 per cent amigen in 10 per cent glucose; (7) 5 per cent pure amino acids in 5 per cent glucose; (8) 15 per cent glucose in water; (9) 15 per cent glucose in 5 per cent amigen; (10) 15 per cent glucose in 5 per cent pure amino acids; (11) isotonic saline solution. Nothing was given orally after the midnight prior to the morning's infusion. The patient voided completely or was catheterized just prior to beginning the intravenous injection. All urine was then saved during the next 4 hour period, including the time consumed by the intravenous infusion. At the end of the 4 hour period, the subject voided completely or was catheterized. Each subject was kept supine in bed, the infusion was set and kept at a steady rate by means of an ordinary intravenous administration set with a screw clamp and was watched during the entire period of administration to insure its constant unchanging rate of drip. No food or drink was allowed during the 4 hour period. For the first 30 injections, 24 hour urine specimens were also saved and examined, but in no case was glucose found to be excreted after 4 hours, so only 4 hour specimens were examined thereafter. The amount of glucose excreted was determined by the quantitative urinary glucose method of Somogyi. Traces less than 0.1 per cent were noted by Benedict's qualitative test.

RESULTS

The relation between glycosuria and the rate of injection of glucose is shown in the scat-

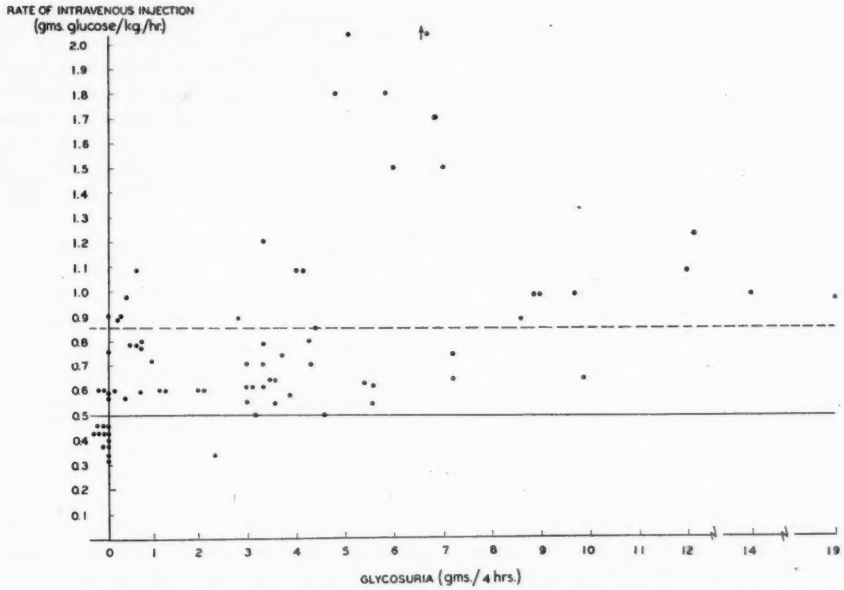


Fig. 1. Glycosuria following intravenous glucose. Each point represents 1 experiment. The horizontal broken line represents the rate set by Woodyatt before which glycosuria occurred. Note only at a rate much lower than this (solid horizontal line) did glycosuria occur in these observations (with 1 exception). Note also a tendency for an increase in the amount of glycosuria with increasing rates of injection.

ter-graph in Figure 1. From this it will be seen that when glucose was injected at rates less than 0.5 gram per kilogram per hour no glycosuria was produced except in 1 instance, whereas at the rates of 0.5 gram per kilogram per hour and above, glycosuria appeared in all but 6 cases. The degree of glycosuria varied considerably among patients and also in single patients when different solutions were given at the same rates. However, the rate at and above which glycosuria appeared was constant (0.5 gm./kgm./hr.) rather than at the figure 0.85 as might have been expected in normal humans, as a result of Woodyatt's observations. The administration of intravenous glucose at the rate of 0.5 gram per kilogram per hour would mean, in practical usage, giving 1 liter of 5 per cent glucose to an average (70 kgm.) person at a steady rate over a period of 1 hour and 25 minutes. One liter of 10 per cent glucose would require a period of 2 hours and 50 minutes, if glycosuria with associated diuretic effect is to be avoided. The findings also suggest a tendency for the amount of glycosuria to increase along with increasing rates of administration of glucose but as indicated in the figure the variations were too wide to draw any conclusions. The amounts of glucose excreted ranged from 0.5 gram up to 12 to 19 grams in a few instances. In general the losses were quite small, ranging from 2 to 6 grams (4 to 12 per cent of the glucose administered), yet they were consistently present and were associated with significant degrees of diuresis.

Total urinary output was measured during the 4 hour period of observation and is shown in Figure 2. The greatest output of urine followed the injection of 5 and 10 per cent glucose in water. The degree of diuresis tended to increase with the amount of glycosuria produced and with the rate of administration but seemed to hold a closer relationship to the type of solution injected. For example, the presence of isotonic saline with 5 and 10 per cent glucose decreased greatly the urinary output.

TABLE II.—EFFECTS OF INTRAVENOUS SOLUTIONS IN A SINGLE PATIENT

Date 1947	Intravenous solution (1,000 c.c.)	Rate of injection gm. gluc. /kgm. /hr.	Amount of urine (c.c.) in 4 hours	Amount of glucose (gms.) excreted
2–9	5% glucose in water	.6	1020	2.1
2–10	5% glucose in 5% amino acids	.6	1170	0
2–11	5% glucose in 5% amigen	.6	810	0
2–12	5% glucose in 5% amino acids	.6	720	trace
2–13	5% glucose in 5% amigen	.6	900	trace
2–14	5% glucose in saline	.6	280	2.0
2–15	15% glucose in water	1.2	1020	30.6
2–16	15% glucose in 5% amino acids	1.2	1020	8.2
2–17	15% glucose in 5% amigen	1.2	1370	20.1
2–20	Isotonic saline	0	240	—
2–23	Isotonic saline	0	280	—

When isotonic saline alone was given an actual hydrating effect was noted, some patients passing as little as 250 cubic centimeters of urine in 4 hours as compared to the usual 600 to 800 cubic centimeters excreted when glucose alone or with saline was administered. The low output of urine with saline is also shown in Table II; 3 injections containing saline produced an output of 280, 240, and 280 cubic centimeters, whereas the glucose injections produced an output of 720 cubic centimeters or more. A mild diuretic effect was noted with solutions containing both amino acids and glucose.

The influence of amino acids on glycosuria was studied in 30 injections in which glucose with hydrolyzed protein (amigen) or pure amino acids were given. Six injections were given at rates below 0.5 gram per kilogram per hour and in no case did glycosuria appear (Table II). Twenty-four injections were given at rates above .5 gram per kilogram per hour (the rate at which glycosuria consistently appeared when glucose alone was given). In 5 of these 24, no glycosuria appeared, and the remaining 19 excreted glucose in comparatively small amounts, ranging from traces to a maximum of 3.8 grams. The presence of amino acids either as such or as hydrolyzed protein (amigen) in some manner effectively reduced the degree of glycosuria as compared with glucose alone given at the same rates. The effect is clearly shown in an experiment carried out in a single patient who was first given concentrated glucose solutions (15 per cent) alone and subsequently in combination with amigen and with pure amino acids administered at the same rates, far above the "threshold" level for glycosuria. A striking reduction in degree of glycosuria was noted when either amino acids or amigen was in the solution (Table II).

With the idea of determining more specifically the nature of the influence of amino acids, experiments were carried out in several subjects in which the blood glucose levels were measured at half-hour intervals during and following the infusion. Higher blood glucose levels were reached when glucose was given alone than when in combination with amino acids; the hyperglycemia paralleled the degree of glycosuria. This fact tends to indicate that the amino acids act by increasing glucose utilization in the tissues rather than by lowering the renal threshold for glucose excretion. At least, it is apparent that the amino acids in some way enhance the removal of glucose from the circulating blood stream. It was also noted that the effect of pure amino acids in producing a lower curve was more pronounced than that of amigen (hydrolyzed protein), which contains polypeptides as well as amino acids (Table II).

DISCUSSION

From this study it is apparent that glucose given to normal humans in a single controlled intravenous injection is utilized at a rate considerably less than that which Woodyatt and his associates concluded to be normal 32 years ago. This variation may possibly be explained by noting a difference in the method of administration employed. In the present experiments, a single liter of glucose solution was given at a steady unchanging rate from the beginning of the injection to its completion. No unnoticed variation in rate could occur, for the infusion was under constant bedside observation during the entire period of administration, to prevent any changes which might result from shifting of the needle, moving of the subject's arm, or other mechanical factors. Woodyatt and associates, on the other hand, began each injection at a rate con-

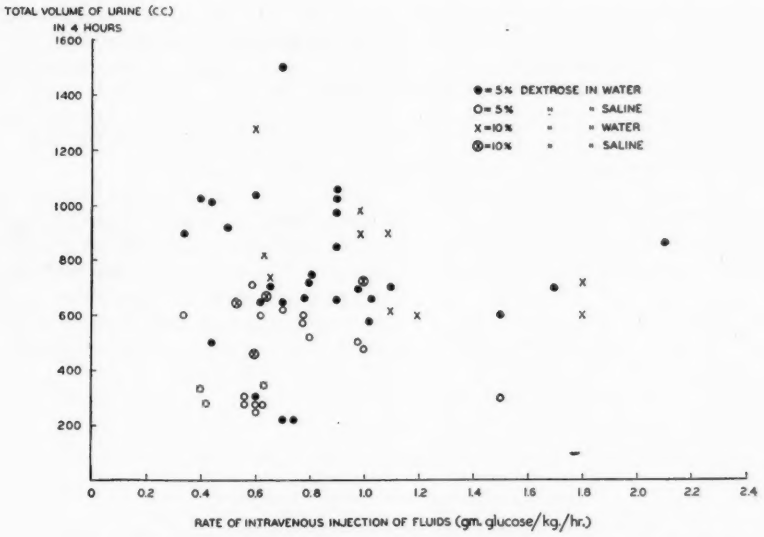


Fig. 2. Urinary output during the intravenous injection of glucose. Each point represents 1 experiment. The effect of saline in reducing urinary output is clearly shown. Note that more than 800 cubic centimeters of urine were excreted only when glucose and water were injected; by contrast less than 400 cubic centimeters were excreted in only 3 cases by glucose and water as compared with 9 cases by glucose and saline. See also Table II in which a similar difference was observed.

sidered to be well below that which would produce glycosuria; this rate was then increased every half hour until glycosuria appeared. Prolonged continuous injections at constant rates followed this initial stepping-up period of administration. It is likely that a lower rate of assimilation would have been observed if Woodyatt had established and maintained a constant lower rate of injection from the beginning, especially since our study revealed that glycosuria often did not appear until the second half hour. It is quite conceivable then that Woodyatt and his coworkers might have exceeded the actual rate of utilization and not detected it because of the frequent latency in the appearance of glycosuria.

It is generally believed also that the utilization mechanism is not a static manifestation and that a "warming up" period is required in order for it to reach its maximum degree of efficiency. Lusk presented the concept that the metabolism of glucose by the tissues tends to increase in the presence of an increased concentration of glucose in the blood stream. Correspondingly, introduction of additional glucose into the blood stream tends to provoke an overproduction of insulin, which then increases the utilization of the subsequent glucose injected. Thus, one may bring about a higher rate of utilization by starting infusions at very slow rates and gradually increasing the speed. However, the application of such a concept to the clinical usage of intravenous glucose presents certain practical difficulties, since fluids ordinarily are given at a more or less constant speed throughout the infusion. The similarity of methods used in this experiment to those in ordinary clinical practice serve to make the findings in this study of practical value.

The hydrating effects of saline, in contrast to the diuretic effects of glucose have been observed by Baxter and by Stewart and Rourke, who administered massive volumes of intravenous solutions over relatively short periods of time (as much as 5 liters in 4 hours). It is interesting to note that similar effects are evident even in single 1 liter injections.

The data herein presented also indicate that the presence of amino acids accelerates the utilization of glucose by the tissues. The mechanism by which this occurs is not immediately apparent and further study is being carried out in an effort to determine the exact nature of this effect. At present one can only conclude (in view of the associated lowered blood glucose curves) that the change is specifically in the utilization mechanism and not the result of an altered kidney threshold.

SUMMARY

1. With normal adult subjects and commonly employed intravenous glucose solutions given at a uniform rate, the maximum speed of injection of glucose without production of glycosuria was found to approximate 0.5 gram per kilogram per hour. This is much lower than the rate of 0.85 gram per kilogram per hour found in normal humans, dogs, and rabbits by Woodyatt and his coworkers. In clinical usage this slower rate of injection should be used when intravenous glucose is administered even to patients in a good state of health, in order to avoid glycosuria and associated diuresis.

2. Urinary output was considerably reduced when isotonic saline was present in the intravenous solution. Higher concentrations of glucose tended to produce more diuresis than lower concentrations, and the amount of diuresis tended to increase with the increased rates of administration.

3. Evidence was obtained that the addition of hydrolyzed protein (amigen) or pure amino acids to the glucose solutions increased the rate of utilization of glucose by the tissues. This was shown by a lower blood sugar level and less glycosuria when amino acids were present than when solutions of glucose alone were given at the same rate.

REFERENCES

1. Baxter, V. C. South. M. J., 1945, 38: 641.
2. Blumenthal, F. Beitr. chem. Phys. Path., 1905, 6: 329.
3. Comessati, G. Beitr. chem. Phys. Path., 1906, 9:67.
4. Fantus, B. J. Am. M. Ass., 1936, 107: 14.
5. Lusk, G. J. Biol. Chem., 1912, 13: 27.
6. Somogyi, M. J. Lab. Clin. M., 1941, 26:1220.
7. Stewart, J. D., and Rourke, G. M. J. Clin. Invest. 1942, 21: 197.
8. Wilder, R. M., and Sansum, W. D. Arch. Int. M., 1917, 19: 311.
9. Winslow, S. B. Surgery, 1938, 4: 867.
10. Woodyatt, R. T., Sansum, W. D., and Wilder, R. M. J. Am. M. Ass., 1915, 65: 2067.

FETAL MORTALITY AND MORBIDITY IN CESAREAN SECTION

S. PEDVIS, M.D., J. K. L. IRWIN, M.D., and N. W. PHILPOTT, M.D., F.A.C.S.,
Montreal, Quebec

DURING the past decade there has been a changing trend in the type of anesthetic agent used for cesarean section at the Royal Victoria Hospital Maternity Division. The following critical survey of fetal mortality and morbidity has been undertaken to compare the results obtained and to study the underlying factors. Cesarean section was performed in 353 cases during the three periods from July 1, 1940 to December 31, 1941, and from July 1, 1944 to July 1, 1945 and from January 1, 1946 to December 31, 1946. These periods were chosen in order to obtain a sufficiently large group of cases of cesarean section carried out under each of the various anesthetic agents. However, the number of sections under general anesthesia is still small, because those before 1940 were not included. Previous to this time the present facilities for blood transfusion and the newer chemotherapeutic and antibiotic agents were not available. For the purpose of this discussion the infants have been classified as follows: (1) normal, those perfectly well at birth who remained so until discharge from hospital; (2) morbid, those who required prolonged resuscitation or had respiratory difficulties, as shown by cyanosis and labored respirations during the first 24 to 48 hours, but who were apparently perfectly well thereafter; (3) dead, nonviable infants, stillborn, or those who died shortly after birth.

The data which lend themselves to statistical analysis are presented in the form of contingency tables and have been tested for independence by calculating X^2 (3). At the foot of each of these tables is the X^2 value, the number of degrees of freedom (n), the probability (P) from Fisher's Table III of X^2 and the odds that the observed differences could arise due to chance alone.

From the Departments of Obstetrics and Pediatrics of McGill University.

In Table I the figures for fetal mortality and morbidity in this series are presented. The term fetal mortality, as pointed out by Irving, has been used to mean gross fetal mortality which consists of (a) nonviable infants, stillbirths, and neonatal deaths, or (b) just stillbirths, or (c) stillbirths and neonatal deaths. In the reports from several large American centers summarized by Irving, the fetal mortality, using the latter definition, ranged from 5.2 to 10.8 per cent. In another group reviewed by Acken the rate ranged from 4.4 to 16.14 per cent; however, he did not define his use of the term fetal mortality. The value of 7.3 per cent for gross fetal mortality or 5.3 per cent for stillbirths and neonatal deaths, in this compilation, compared favorably.

The causes of fetal mortality are enumerated in Table II. It is apparent that prematurity[1] and atelectasis play a major role in causing fetal death. This is in accord with Kohn's series. The large number of premature births in this group can be partially explained by the fact that the indication for cesarean section has made it necessary for the operation to be performed at varying periods before term.

Table III shows the kind of anesthesia that was used in these cases. Since prematurity in itself is such an important factor in fetal mortality the results have also been computed omitting all premature births. The term general anesthesia refers to the employment of (a) cyclopropane or (b) nitrous oxide and ether. In all of these some premedication was given 1 to 2 hours before operation and consisted of one or a combination of the following: atropine, scopolamine, heroin, morphine, barbiturates. Spinal anesthesia refers to a single injection of 1 per cent pontocaine in conjunction with ephedrine hydrochloride ¾ grain

[1]Prematurity includes all infants weighing less than 2500 grams at birth. In a small number of cases (macerated fetus) no weight record could be found; if the period of gestation was 7 months or less, these were also included as premature births.

TABLE I.—FETAL MORBIDITY AND MORTALITY FOLLOWING CESAREAN SECTION

No. cases		Normal		Morbid		Total dead		Stillbirths and neonatal deaths	
Sections	Fetuses	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
353	357	289	80.9	42	11.8	26	7.3	19	5.3

subcutaneously 15 minutes before and ¾ grain repeated immediately before the spinal injection. Local anesthesia refers to the use of 1 per cent novocain. From these figures it appears that general anesthesia gives a slightly higher fetal morbidity, and local anesthesia a lowered fetal morbidity but a higher mortality. However the differences are not regarded as significant. The anesthetic agent of choice must not only be most favorable to the fetus but also to the mother. In this series there was only 1 maternal death. The patient had a local anesthetic and death was attributed to uterine hemorrhage. It is of interest that in the last 500 patients who had a spinal anesthetic for cesarean section at the Royal Victoria Maternity Hospital there was only 1 maternal death (6).

The results for full term stillbirths and neonatal deaths are similar to those of Irving. Our results are listed in parentheses after his for the following types of anesthesia: general, 4.4 per cent (1.9 per cent); spinal, 4 per cent (2.2 per cent); local, 9.7 per cent (4.1 per cent). Allen and Slocum using cyclopropane in 120 cases reported a fetal mortality of 2.5 per cent and a morbidity of 16.7 per cent. Torrie reviewed 120 sections done under spinal anesthesia with 1 per cent pontocaine and obtained a fetal mortality of 5.8 per cent.

TABLE II.—CAUSES OF FETAL MORTALITY

Causes	No.	Per cent	No.	Per cent
Prematurity alone	2	4.8	15	36.6
Prematurity associated with other causes	13	31.8		
Atelectasis alone	5	12.2	12	29.3
Atelectasis associated with other causes	7	17.1		
Congenital abnormalities	5	12.2		
Deadborn, macerated	4	9.8		
Erythroblastosis fetalis	2	4.8		
Hemorrhage—cerebral, subarachnoid	2	4.8		
Aspiration mucus plug	1	2.5		

TABLE III.—KIND OF ANESTHESIA IN RELATION TO THE FETAL CONDITION

Anesthetic used for mother	No. cases	Fetus					
		Normal		Morbid		Dead	
		Observed	Expected	Observed	Expected	Observed	Expected
Spinal	229	184	185	30	27	15[1]	16.7
General	54	41	44	10	6.3	3[2]	3.9
Local	74	64	60	2	8.7	8[3]	5.4
		X^2=9.7751; n=4; P=.05; odds 1:19					

[1]Includes 10 premature births
[2]Includes 2 premature births
[3]Includes 2 premature births

Table IV records the type of anesthesia in relation to the various indications for cesarean section. It is obvious that the higher number of toxemias and medical indications for section in the local group could account for part of the increased fetal mortality. However, there is a higher number of cases with placenta previa in the general group, and of Rh incompatibility and elderly primipara in the spinal group to

TABLE IV.—TYPE OF ANESTHESIA IN RELATION TO INDICATION FOR CESAREAN SECTION

Indications for cesarean section	Type of Anesthesia					
	Spinal		General		Local	
	No.	Per cent	No.	Per cent	No.	Per cent
Disproportion	97	43.1	20	37.1	32	44.5
Placenta previa	22	9.7	7	13.0	8	11.1
Repeat section	40	17.6	9	16.7	12	16.7
Elderly primipara	13	5.7	2	3.6	0	0
Inertia	4	1.7	1	1.9	0	0
Toxemia	7	1.7	2	3.6	8	11.1
Rh incompatibility	6	3.0	0	0	0	0
Uterus—bicornuate, rupture, prolapse, fibroids	17	7.5	5	9.3	5	6.9
Medical—diabetes, nephritis, carditis, psychosis	10	4.4	2	3.6	5	6.9
Retroplacental hemorrhage	3	1.3	1	1.9	0	0
Previous endometriosis miscarriages, difficult labor. Inversion elective	8	3.4	5	9.3	2	2.8

TABLE V.—KIND OF ANESTHESIA IN RELATION TO THE FETAL CONDITION IN CASES OF DISPROPORTION

Anesthetic used for mother	No. cases	Fetus					
		Normal		Morbid		Dead	
		Observed	Expected	Observed	Expected	Observed	Expected
Spinal	96	88	86.3	8	9.1	0	.64
General	20	16	18.0	4	1.9	0	.14
Local	32	29	28.7	2	3.0	1	.22

$X^2=6.7122$; n=4; P=.2; odds 1:4

account for part of their increases. Therefore, in an attempt to find a group that would be more strictly comparable, the type of anesthesia in relation to the fetal condition has been analyzed in the cases in which disproportion was the only indication for section (Table V). Although fewer cases are considered than in Table III the same general conclusions appear to hold.

In Table VI an attempt is made to evaluate the effect on the fetus of the type of premedication used for the mother. The cases of spinal, general, and local anesthesia in which the fetus did not have the special management described in the following have been included in this study. It would appear that the opiates given to the mother increase fetal mortality; this is probably due to the narcotic effect on the fetus

TABLE VI.—TYPE OF PREMEDICATION USED FOR THE MOTHER IN RELATION TO THE FETAL CONDITION

Premedication used for mother	No. cases	Fetus					
		Normal		Morbid		Dead	
		Observed	Expected	Observed	Expected	Observed	Expected
Morphine or heroin or opiate plus barbiturate	27	22	22.9	2	3.3	3	0.8
Atropine plus hyoscine or atropine plus barbiturate	50	43	42.5	6	6.1	1	1.4
Barbiturate	10	10	8.5	0	1.2	0	0.3
Ephedrine	71	56	60.3	14	8.7	1	2.0
Opiate plus atropine or hyoscine	40	36	34	4	4.9	0	1.1
No premedication	15	14	12.7	0	1.8	1	0.4

$X^2=15.0961$; n=10; P=0.2; odds=1:4

Fig. 1. A tilt table designed to lower the baby's head at any angle when the infant needs resuscitation; the rocker method may be employed to tilt the baby up and down.

and the consequent depression of the respiratory mechanisms. However, there is no significant difference between the treatments, particularly in view of the fact that a certain bias exists in the indication for the type of premedication.

The high fetal mortality and morbidity rates particularly due to atelectasis in cases of cesarean section prompted the members of the pediatric service in January, 1946 to suggest that all these infants be postured with head down perpendicularly for ½ hour after birth and that at the same time the excess mucus be

TABLE VII.—FETAL CONDITION IN RELATION TO USE OF SPECIAL MANAGEMENT OF INFANT IMMEDIATELY AFTER BIRTH.

Anesthetic used for mother	Fetus					
	Normal		Morbid		Stillbirths and neonatal deaths	
	Observed	Expected	Observed	Expected	Observed	Expected
Special management used, 127	105	101.2	16	18.7	6[1]	6.9
Special management not used, 75	56	59.8	14	11.3	5[2]	4.1

$X^2=1.7343$; n=2; P=.5; odds 1:1.9
[1]Includes 4 premature births
[2]Includes 3 premature births

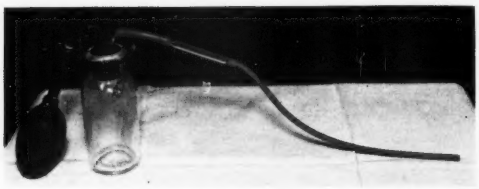


Fig. 2. Hand suction apparatus which prevents contamination ordinarily caused by mouth suction. There is an outlet valve on the end of the rubber bulb.

aspirated from the mouth and pharynx. The latter permits drainage of amniotic fluid and mucus from the respiratory tract and so tends to prevent obstruction by these materials. It was also suggested that oxygen be administered intermittently by mask under positive pressure in an attempt to aid expansion of the fetal lung tissue and to improve oxygenation of the blood. In Table VII two groups similar in all respects except for this special management of the infants are compared. The trend in the data is in favor of this special management but the difference is not significant.

The fetal deaths have been analyzed in relation to the indications for section in the mother and are shown in Table VIII. Fifty per cent occurred in instances in which placenta previa was the reason for section. This emphasizes the importance of hypoxia as a result of maternal blood loss in fetal mortality. The significance of preventing a sudden drop in blood pressure under spinal anesthesia which may impose the deleterious effects of hypoxia in both mother and fetus and the administration of ephedrine to ameliorate this condition is emphasized in Torrie's article.

TABLE VIII.—FETAL DEATHS IN RELATION TO INDICATION FOR CESAREAN SECTION

Indication for cesarean section	Fetal deaths	
	No.	Per cent
Placenta previa	13	50.0
Rh incompatibility	3	11.5
Repeat section	3	11.5
Toxemia	3	11.5
Chronic nephritis	2	7.7
Chronic carditis	1	3.9
Disproportion	1	3.9

Fig. 3. Baby being resuscitated on the tilt table which is placed in the heated cot. Note the legs fastened by means of cotton bandage. The hand suction is also being used to clear the air passages.

While these data have not shown a significant difference between treatments, the consistency of the direction of the trend has prompted us to continue this study and to suggest that in order to reduce fetal mortality and morbidity in cesarean sections general or spinal anesthesia without premedication but with the special management of the infants be utilized. With a general anesthetic when the uterus is opened the maternal respiratory system should be cleared of all anesthetic gases and 100 per cent oxygen be given to prevent hypoxia in the fetus. When spinal is used, particular care should be taken to prevent any wide fluctuation in the maternal blood pressure. In cases in which placenta previa is the indication for section, blood transfusions should be given to the mother preceding or during the operation to maintain her blood volume and so prevent hypoxia in the fetus. Since prematurity is a prime factor in causing fetal death the operation should be delayed as long as possible con-

sistent with the particular indication for cesarean section.

The following routine is recommended in handling infants delivered by cesarean section:

1. Have a pediatrician present to receive the infant from the obstetrician.

2. Place the infant in a heated crib and cover with a previously warmed blanket.

3. Hold the infant perpendicularly with the head down for 20 to 30 minutes or tie the infant to a tilt table as designed by one of the authors (Fig. 1). This is particularly useful when the infant needs resuscitation since the "rocker method" may be employed by tilting the table up and down. Oxygen can be given by mask at the same time.

4. Aspirate the mucus and amniotic fluid from the nose, mouth, and pharynx. One may use a rubber catheter with a glass trap. However, this has the disadvantage that occasionally bacteria from the doctor's upper respiratory passages may reach the infant and vice versa. One of the authors has designed a hand suction apparatus (Fig. 2) which prevents this difficulty. These are used in preference to the various mechanical suction types of apparatus which are connected to the resuscitation machines because we have found the strong suction in the latter can injure the oral and pharyngeal mucous membrane of the infant. The frequent application of the catheter to the posterior pharynx may also initiate vomiting. If this occurs when the doctor is present he can remove the fluid, whereas if it should occur when the infant is alone in its crib some of the vomitus may be aspirated into the lower respiratory tract.

5. Administer oxygen intermittently by mask.

6. Perform routine care such as the administration of vitamin K intramuscularly and the instillation of silver nitrate solution to the eyes.

7. Return all infants to the premature ward for careful observation and tilt the crib to an angle of 45 degrees and place the infant in crib so that the head is at the lower end for a period of 12 hours.

SUMMARY

1. In 357 infants delivered by cesarean section the gross mortality was 7.3 per cent and the morbidity 11.2 per cent.

2. Of the fetal deaths, prematurity and atelectasis accounted for 36.6 and 29.3 per cent respectively.

3. Fetal mortality in cesarean section was high due to the maternal complications which necessitated the operation. Spinal anesthesia has not appreciably affected the fetal mortality but it has definitely lowered maternal morbidity and mortality.

4. Disproportion was the principal indication for section.

5. Premedication in the form of morphine, heroin or ephedrine appeared to have an adverse effect on the fetus, but the difference was only slight.

6. Special management of the infant at birth tended to reduce the fetal mortality and morbidity.

7. Of the fetal deaths, 50 per cent occurred in those cases in which placenta previa was the indication for section.

8. A method for handling infants born after cesarean section is described.

REFERENCES

1. ACKEN, H. S. Am. J. Obst., 1947, 53: 927.
2. ALLEN, C. L., and SLOCUM, H. C. Texas J.M., 1946, 42:482.
3. FISHER, R. A. Statistical Methods for Research Workers. 7th ed. London: Oliver and Boyd, 1938.
4. IRVING, F. C. Am. J. Obst., 1945, 50:660.
5. KOHN, S., et al. West Virginia M. J., 1945, 41:49.
6. PHILPOTT, N. W. Personal communication.
7. TORRIE, A. M. Anaesthesiology, 1945, 6:154.

PROLAPSE OF REDUNDANT GASTRIC MUCOSA

ARTHUR M. COVE, M.D., and WILFRED C. CURPHEY, M.D., M.S., F.A.C.S.,
Stockton, California

IN the past the presence of hypermobile redundant gastric mucosa has been such a common and incidental finding by surgeons and roentgenologists, that little significance was placed upon it as an etiological factor. Consequently, no attempt was made to correct the condition. Since Scott in a recent article gave impetus to the study of this problem, more and more writers are beginning to recognize its significance as a clinical entity and as the cause of many otherwise unexplained gastrointestinal complaints. It is difficult to understand why this condition should have been so universally overlooked in the past in patients with gastrointestinal disease.

Bockus still believes that only severe prolapse associated with gastritis can cause symptoms and then, only after producing partial pyloric obstruction. He also feels that gastric symptoms from this source are so rare that they have no practical significance. Others also believe that this lesion is of no particular significance and some roentgenologists do not report this abnormality. On the other hand, Melamed (4) has collected 25 cases of prolapsus with symptoms, all relieved either by medicine or surgery.

During the past year we have observed no less than 22 such patients with symptoms which were otherwise unexplained, 5 of whom came to surgery. All 5 patients operated upon have experienced relief from symptoms, and a more detailed analysis will be given later. In 1926, Eliason, Pendergrass, and Wright first described the roentgen signs produced by prolapse of gastric mucosa. In Melamed's (7) original article in 1943 he was able to find only 19 proved cases in the literature and published a report of 1 case of his own, a total of 20 cases. On the other hand, Archer states that prolapsing gastric mucosa is not rare, but he gives no figures. Feldman indicates that redundant gastric mucosa occurs in approximately 1 per cent of all patients with gastrointestinal tract disease and points out that the condition is not recognized until mucosa prolapses into the pyloric canal or into the duodenal cap. In Scott's survey of this problem 19,228 hospital admissions were analyzed. Roentgenological examinations of the upper gastrointestinal tract were made in 1,346 of these patients which revealed the presence of: gastric ulcer in 13 or 0.96 per cent; duodenal ulcer in 325 or 24.1 per cent; duodenitis in 17 or 1.3 per cent; prolapse of redundant gastric mucosa in 14 or an incidence of 1.04 per cent; gastric tumors in none. In our series of patients upon whom an upper gastrointestinal tract examination was made the incidence of prolapse of gastric mucosa was even greater. A review of 650 consecutive examinations revealed that prolapse had occurred in 22 cases, a percentage of 3.38. This corroborated our original impression that the incidence is greater than usually suspected.

In the past prior to the development of our interest in the presence of this lesion this diagnosis was overlooked in many cases because: first, the examiner was unaware of the significance of the finding; second, filling defects produced by prolapse were confused with those due to other conditions; and third, when recognized, the condition was believed to be of no clinical importance and an attempt was made to explain the clinical symptoms on some other basis.

From Curphey Clinic, Stockton, California, and San Joaquin General Hospital, French Camp, California.

SYMPTOMATOLOGY AND PHYSICAL FINDINGS

Patients with prolapse of redundant gastric mucosa complain of a variety of symptoms which usually are influenced by the extent and the condition of the prolapsed mucosa. These symptoms are never characteristic and do not permit a clinical diagnosis of the disorder. As a general rule the diagnosis must be made on

the basis of roentgenologic findings after elimination of the presence of all other gastrointestinal lesions. Likewise, the objective physical findings are indecisive with the exception of a palpable tumor mass in the epigastrium in the region of the pylorus. Such a mass is characterized by its soft, doughy consistency associated with free mobility and with a very characteristic sensation to the examining fingers when the prolapse is reduced. This palpable quality can be likened only to that of a hernia during the process of reduction under the palpating fingers. This sensation no doubt is caused by the sliding of the prolapsed gastric mucosa back through the pyloric ring, and its finding on physical examination is pathognomonic of the lesion just as the similar findings of a soft tumor mass in the groin which can be reduced back into the abdominal cavity through a small defect in the abdominal wall with a mucous gurgling sensation is pathognomonic of hernia. In 2 of our patients reported in this series this finding was present on numerous occasions. And in each case immediately after the reduction of the prolapsing mucosa through the pyloric ring by the examining fingers, the palpable tumor could no longer be demonstrated.

The only other physical finding of any consequence is the occasional presence of mild tenderness in the region of the pylorus which, of course, is an incidental finding and may be associated with numerous lesions in this region.

The major symptoms therefore, of which these patients complain are: intermittent epigastric distress with cramping pains, no doubt based on partial pyloric obstruction; varying relationship to food; sense of fullness, bloating, and heart burn; nausea and vomiting; gastrointestinal hemorrhages. The disorder should be suspected in any patient with an atypical ulcer history in whom there is not a satisfactory response to ulcer regimen, and in those with repeated recurrences when placed on solid foods as well as in those with recurrent functional complaints and with recurrent small or large gastrointestinal bleeding which cannot be explained on any other basis.

As a general rule, the routine laboratory examination of the blood and urine reveals no abnormality. Secondary anemias due to prolonged intermittent bleeding may be found in some patients. Scott reports that in over two-thirds of the patients gastric analyses show results within normal limits; in one-third hyperchlorhydria is revealed. Persistent occult blood in the stools may be found in many of these patients.

Gastroscopic examination was done on one of our patients and no abnormality discovered. Similarly, those who report the findings on gastroscopy do not indicate that any significant evidence may be obtained by this method. However, the principal value of gastroscopy in these cases lies in the ruling out of other gastric lesions which may be missed by roentgen examination.

DIAGNOSIS BASED ON ROENTGENOGRAPHIC FINDING

The diagnosis of prolapse of the gastric mucosa into the duodenum should be suspected from the clinical history and, on occasion, from the physical findings. However, the appearance at fluoroscopy and on examination of the roentgen films is quite characteristic and the condition is easily recognized by the roentgenologist if the pathology of the disorder and the following features are kept in mind.

Characteristically prolapse of redundant gastric mucosa into the duodenal bulb is represented by a central filling defect near the base of the bulb, most often lobulated. This gives a mushroom or cauliflower-like appearance which may vary somewhat in extent and configuration on the same and different examinations. In our experience the defect has been more readily demonstrated in the horizontal than the erect position. In most instances the defect is traversed by lines of increased density which can be followed into the stomach and are continuous with the gastric rugae. In uncomplicated cases the outline of the bulb is smooth and fluoroscopically no irritability or spasm is noted. Point tenderness has not been a frequent finding. In several of the cases some narrowing of the pylorus has been noted suggesting hypertrophy. Although seen in a number of the cases, hyperperistalsis has not been constantly associated. There were no craters seen, and no patients had gastric

Fig. 1. Case 1. Large central defect at the base of the bulb producing a mushroom-like appearance. The gastric rugae can be traced into the defect.

residue at 6 hours. It is well to attempt to classify the degree of prolapse (mild, moderate, and marked) as this may be of some clinical value.

Differential diagnoses. (1) Prolapsing polypoid tumor of the pyloric end of the stomach. It is possible that at times a definite differentiation cannot be made. The tracing of the rugal fold into the defect, however, should aid considerably in establishing the diagnosis. Also, in prolapse there will be no defect seen at any time on the gastric side of the pylorus. (2) Hypertrophy of the pyloric sphincter. In this condition there is a curved pressure defect on the base of the duodenal bulb, but no area of radiolucency is seen. The umbrella appearance which has been described in this lesion has been found to be present in prolapse more frequently than one would expect normally. This is probably due to the fact that in prolapse, hypertrophy of the pylorus takes place. (3) Duodenitis. As has been mentioned before, the lack of spasm and irritability of the bulb should establish the differentiation. Likewise, instead of the rugal pattern being enlarged and irregular, it is more apt to be compressed. (4) Duodenal ulcer. In prolapse the margins of the bulb are smooth, even in cases of marked degree. In our present series there have been 2 cases of associated duodenal ulcer and prolapse of gastric mucosa. In 1 of these, a gastroenterostomy was performed 20 years previously for the ulcer. When these two conditions coexist, in addition to the central defect, one notes a deformity of the contour of the bulb or a crater. (5) Hypertrophic gastritis. In this condition the enlarged gastric rugae may enter the bulb, but in addition to evidence of disease in other portions of the stomach, gastroscopy should readily reveal the true nature of the condition. (6) Polyp of the duodenum. These are infrequently found. When present they may be in other places than at the base of the bulb. The gastric rugae will not be traced into the defect.

In the past, it is probable that prolapse has masqueraded as one of the above conditions, mainly because we have not been alert and aware of this entity. The roentgenologic appearance, however, is sufficiently characteristic to establish the diagnosis.

TREATMENT AND RESULTS

Treatment of the vast majority of these patients may satisfactorily be confined to medical measures, and in slight and moderate prolapses frequent small feedings of a bland diet usually afford relief. In some, hospitalization, rest in bed, and freedom from tension associated with the elimination of all condiments, as well as, tobacco, alcohol, and caffeine will effect some degree of relief from distress. On the other hand, there is little reason for one to assume that such relief will be permanent. Although the etiology of this lesion is not clear, the pathology is definite enough for one to conclude that the lesion is purely on a mechanical basis and once established will in all probability receive no permanent relief short of mechanical correction. Regarding the etiology and pathology of the

lesion, many factors have been suggested which may contribute to its occurrence. An enumeration of these factors may be set down as follows: first, the presence of a small unrecognized mucosal ulcer which results in the hyperplasia of the gastric mucosa (Bralow and Melamed, 4); second, the presence of hypertrophic gastritis (Bockus); third, persistent hypermotility of the stomach; and fourth, congenital variation in the anatomy of the stomach structure consisting of a gastric mucosa which is abnormally hypermobile on the surface of the gastric muscularis.

All of these factors seem to be adequately summarized by Scott who points out that the one common denominator in the theories regarding the etiology of prolapse is an abnormal disturbance of gastric peristalsis and function. The most common, continuous, and effective means of altering gastric functions springs from the effects of emotions and the nervous system on gastric motility. Consequently, in view of the construction of the stomach walls which normally permit some degree of mobility between them, it seems possible that certain neurogenic factors are the inciting cause of a disturbed gastric function that ultimately brings about a mucosal prolapse. This fact becomes more possible when one bears in mind that secretory as well as motor activities of the stomach are definitely correlated through Meissner's plexus located in the submucosal coat of the stomach. The pre-existing disease process of the gastric mucosa is not necessary for the production of a prolapse. Melamed is inclined to support this theory and indicates that since the muscularis mucosa is known to have muscular activity independent of that of the main musculature of the stomach, it is entirely possible that neurogenic factors are the inciting cause of a disturbed gastric function that ultimately brings about a prolapse. He further points out that it has been repeatedly shown that emotion, such as, worry, fear, excitement, and anger alter not only gastric chemistry but also peristalsis.

In considering the fourth and most important factor in the etiology of the lesion, namely, the abnormal hypermobility of the gastric mucosa on its muscularis which may

Fig. 2. Case 2. Large lobulated defect in the bulb, but the contour of the bulb is maintained. Appearance is similar to that of polypoid growth.

be either a congenital characteristic or an acquired lesion, Melamed points out the following facts. In the first place, in the normal gastric antrum the mucosa and muscularis are connected by soft yielding submucosa composed of loose areolar tissue containing blood vessels, lymphatics, and nerves. This explains a certain amount of limited mobility of the mucosa on the muscularis as is found in all normal stomachs and may be easily demonstrated at autopsy. Scott points out that in his study of over 100 fresh stomachs normally the extent of this movement was not sufficient to permit a prolapse, and that in those few cases in which a prolapse could be produced the previous history of the patients indicated that they actually had had gastric symptoms. Melamed was not able to confirm this observation since in several cases which he witnessed the gastric mucosa could be pulled

Fig. 3. Case 3. Large central defect in the duodenal bulb. The gastric rugae are well demonstrated passing through the defect.

Fig. 4. Case 4. Irregular filling defect at the base of the bulb producing a cauliflower appearance.

through the pylorus with a forceps, and he intimated that a gastric mucosa could be pulled through to correspond with Scott's description of a small prolapse.

Obviously, the lesion then is a mechanical one based on a hypermobility of the gastric mucosa which may be congenital in nature or may have been produced by abnormal gastric motility which over a period of time loosens the attachment of the mucosa to the muscularis to such an extent that a prolapse can occur. In all probability, such a lesion cannot correct itself but must be corrected by mechanical means, such as removal of the redundant mucosa or adequate anchorage of the mucosa to the muscularis.

This does not preclude that all such patients must be treated surgically since a vast majority of them can live comfortably and without symptoms by simple medical management, as previously pointed out. We must, therefore, consider the logical indications which justify surgical treatment. The essential factors which influence a decision with respect to the advisability of surgery are, first, the persistence, severity, and intractability of symptoms. In other words, if the symptoms are persistent and intractable to medical management, the patient as well as the surgeon will in all probability be inclined to seek more drastic means of relief. The second essential factor is that of pyloric obstruction to the extent that recurrent persistent vomiting may occur which is associated with the failure of the patient to maintain his normal weight. Obviously, such a lesion is disabling and interferes with the body physiology to the extent that partial starvation is present. It therefore warrants the risk of surgical intervention for its correction. The third essential factor, one we believe important, is repeated gross gastrointestinal hemorrhages experienced by an occasional patient, or a secondary anemia resulting from repeated small bleeding. Such patients obviously require surgical correction of the lesion since hemorrhage can occur to such a great extent as to endanger life. In 2 of our patients such a problem was present.

SURGICAL ASPECTS

a. Surgical correction of these lesions is usually accomplished by resecting a generous portion of the redundant gastric mucosa following which some type of an adequate pyloroplasty is done. Such a procedure is recommended by Bohrer and Copleman. Rees recommends not only antral gastrostomy with excision of the redundant mucosa and pyloroplasty but also anchorage of the mucosa to the muscularis and section of the pyloric muscle. A similar type of procedure is suggested by Archer and Cooper, Scott, and Bralow and Melamed. Recently more radical procedures have been suggested. Norgore, Martin, and Schuler reported 2 instances in which they did a Finsterer type of retrocolic enterogastric anastomosis following a partial resection of the stomach. In our patients who came to surgery the procedure has been one of antrotomy with division of the pyloric muscle resection of an abundant portion of the prolapsing gastric mucosa followed by a Horsley pyloroplasty or Finney pyloroplasty. We have not felt justified in doing the more radical procedure of partial gastric resection.

b. Findings at operation. Upon celiotomy in a case of suspected prolapse of the redundant gastric mucosa it is essential that certain findings be present before one is justified in carrying out an extensive surgical procedure. The following exploratory maneuvers are done before a final decision is arrived at. First, the stomach is adequatcly exposed, and the pylorus and duodenal bulb are gently palpated. In most cases, if prolapse is present, a soft doughy mass is distinctly palpable in the duodenal bulb. By gentle taxis this mass is reduced through the pylorus into the stomach and can be reproduced by a gentle milking action on the pyloric end of the stomach. Such a finding is pathognomonic of the lesion. On the other hand, if palpation of the stomach reveals a prominent folded gastric mucosa in the pylorus which does not at the time produce an actual prolapsing mass into the duodenal cap, one is justified in doing an antrotomy. The gastric mucosa is then tested for hypermobility by securing a fold of the mucosa by means of the forceps placed well above the pyloric sphincter. By this means a hypermobile gastric mucosa may be easily pushed through the pyloric sphincter into the duodenal cap and may readily produce a typical prolapse. If this finding is present one is justified in resecting a generous portion of the mucosa which is readily done by raising a large fold of the posterior gastric mucosa between two Allis forceps and applying a clamp at the base of this folded mucosa longitudinal to the axis of the stomach and crossing the pyloric sphincter. The cut edges of the mucosa are then approximated by atraumatic catgut suture which may on occasion include a small portion of the gastric muscularis so that adequate anchorage is effected.

ANALYSIS OF CLINICAL ASPECTS IN OUR CASES

Analysis of the clinical aspect in 20 cases (2 ulcer patients excluded) revealed: The average age was 49 years; the youngest being 26, the oldest 64. Fourteen were males; 6 were females. Twelve were obese; 5 were slightly overweight. Eighteen were white, 2 negro. History of overindulgence of alcohol was present in 5 cases.

The average duration of symptoms was 2 to 3 years. Abdominal pain or discomfort was the most common complaint. This varied considerably both as to type and location. Pain was relieved by food in 4, aggravated in 8, not related in 5, and indefinite in 3. Seven stated that pain was aggravated by fatty foods, spices, and alcohol. Vomiting was a prominent symptom in 3 cases, fairly frequent in 4. There was a history of more than 3 massive bleeding episodes in 2 cases; 3 others gave a history of hematemeses or tarry stools.

RELATION OF SYMPTOMS TO DEGREE OF PROLAPSE

There were 6 cases classified as mild prolapse, 7 as moderate, and 7 as marked. In the patients whose symptoms were controlled poorly by diet 4 had marked prolapse, 2 moderate, and 1 mild. As to severity of symptoms, in the 6 cases classified as mild prolapse, 5 patients had vague complaints; in the 7 cases of moderate prolapse, 5 patients had bothersome symptoms; 6 of the 7 patients with severe prolapse had severe symptoms. (The remain-

ing patient's only complaint was repeated gastrointestinal hemorrhages.)

CASE HISTORIES

CASE 1. F. S., 45 year old white male, complained of pain in the upper abdomen of several years' duration. The pain consisted of recurring cramps following meals. Other history was essentially negative. Patient did not respond to a medical regimen. He was operated on and a resection of redundant gastric mucosa associated with Finney type of pyloroplasty was performed. Patient has now been free of complaints for 1 year.

CASE 2. C. N., 35 year old female, had repeated attacks of nausea and pain in the upper abdomen of 4 to 5 years' duration. In the past few months she had developed nocturnal vomiting. The pain was aggravated by food intake, particularly solid foods. There was some weight loss. The patient was operated on, a large quantity of redundant gastric mucosa was removed and a Finney type pyloroplasty was performed. Following operation gastric complaints disappeared. The patient has gained weight as a result of her ability to eat any type of food.

CASE 3. W. C., 32 year old negro male, had a 4 year history of burning pain in the epigastrium occasionally relieved by food, occasionally aggravated by food. Gas and sour stomach were also present. Vomiting occurred at infrequent intervals. There was a history of several episodes of frank hematemesis and tarry stools. In the past he had been told he had a duodenal ulcer and had received some benefit from an ulcer diet. Following operation (resection of redundant gastric mucosa and pyloroplasty), the patient had complete relief from symptoms. (Incidentally, no ulcer was found at operation.) Six months later the patient returned with a history of vague abdominal distress for 2 to 3 days followed by hematemesis and tarry stools. Gastrointestinal series at this time revealed a deformed bulb and pylorus which was considered to be secondary to the pyloroplasty. Hemorrhage may have been due to a shallow ulcer at the suture line. The patient treated conservatively has been symptom free for 3 months.

CASE 4. D. M., 61 year old white male, has been suffering from generalized rheumatoid arthritis for many years. He had a history of massive hematemesis 6 times in the last 5 years. Numerous previous gastrointestinal studies were said to be negative. There were no other gastrointestinal complaints. The patient was operated on and resection of redundant mucosa and Horsley pyloroplasty were performed. It has been only 3 months since operation. The patient states, however, that he can now recognize that he did have some abdominal distress prior to the operation which is no longer present.

CASE 5. T. B., 54 year old female, complained of stomach trouble for the past 4 or 5 years. Pain was present in the upper abdomen aggravated by food intake. No relief was obtained from diet or other medical measures. The patient was operated on, redundant gastric mucosa existed, and a Heineke-Mikulicz pyloroplasty was performed. Since the operation, the patient has been entirely free of symptoms.

CONCLUSIONS

1. Prolapse of gastric mucosa is more common than generally suspected.
2. The diagnosis can only be established roentgenologically, since the clinical picture is extremely variable.
3. Mild degrees of prolapse rarely produce symptoms and probably are only an incidental finding.
4. Moderate or marked degrees of prolapse are often associated with complaints of sufficient severity to cause the patient some degree of disability.
5. The most common complication of prolapse is gastrointestinal hemorrhage.
6. The symptoms of prolapse can be controlled medically in the majority of instances.
7. With symptoms of sufficient degree failure of response to medical treatment is an indication for surgical treatment. Surgery is also indicated in those patients who have had repeated severe gastrointestinal hemorrhage.
8. The surgical procedure of choice is the simplest which will correct the lesion—antrotomy with removal of redundant gastric mucosa combined with some type of pyloroplasty.

REFERENCES

1. ARCHER, V. W., and COOPER, G., Jr. South. M. J., 1939, 12: 252.
2. BOCKUS, H. L. Gastroenterology, 1946, 1: 762.
3. BOHRER, J. V., and COPLEMAN, B. Radiology, 1938, 31: 220.
4. BRALOW and MELAMED. Am. J. Digest. Dis., 1947, 14: 215–221.
5. ELIASON, PENDERGRASS, and WRIGHT. Am. J. Roentg., 1926, 15: 295.
6. FELDMAN, M. Clinical Roentgenology of the Digestive Tract, 2nd ed., p. 155. Baltimore: The Williams & Wilkins Co., 1945.
7. MELAMED, A., and HILLER, R. I. Am. J. Digest. Dis., 1945, 10: 93.
8. NORGORE, MARTIN, and SCHULER, IVAN J. D. Surgery, 1945, 18: 452.
9. REES, O. E. Surg. Gyn. Obst., 1937, 64: 689.
10. SCOTT, W. G. Radiology, 1946, 46: 547.

INDURATED LEG AND LEG ULCERS

A Clinical Study of Their Etiology and Treatment

HOWARD MAHORNER, M.D., F.A.C.S., New Orleans, Louisiana

THE purpose of this presentation is to record conclusions and opinions on indurated leg and leg ulcer arrived at after a large experience over a period of some 20 years in the management of vascular diseases affecting the lower extremity. Included in this clinical experience are numerous cases of varicose veins, indurated legs, leg ulcers, thromboangiitis obliterans and other vascular diseases. After many years of working with these problems one is bound to reach certain crystallized conclusions at times conflicting sharply with views frequently expressed in the literature, at other times in perfect agreement with commonly recorded doctrine.

An attempt will be made to present the subject as a composite problem intensely complex and including all the various factors which might influence the lower extremity ultimately to become the seat of some pathologic process which leads to induration and then ulceration. When any individual problem of this sort presents itself the potentialities of its causes and treatment, if viewed broadly and more or less completely, will help in its solution. Each individual problem is usually very intricate, and does not represent merely one phase without variations or influencing factors other than those immediately apparent. It is important to think of these problems in a projected fourth dimension; not only what the leg looks like objectively now, but what it will look like in 15 or 20 years unless certain component causes which have influenced it and which will continue to influence it in the future are changed. When one sees a small leg ulcer, particularly on a young individual or a postthrombophlebitic edema 2 months after a deep vein thrombosis has occurred, it is helpful to think of other cases of this type but 15 years farther advanced. Thus the course of the new case of postthrombophlebitic edema may be projected into the future with its complications and end-results. With such consideration it is possible to envision various measures and advices which may be given to prevent as far as possible the development of more advanced stages of the same process.

If a doctor is to manage such a problem in an optimum manner, not only must he have knowledge of the various therapeutic measures which may be employed, but he must view even the minor processes, such for example as varicose veins with a little scaly dermatitis near the internal malleolus, not only as a stationary pathologic condition but as one whose factors will continue to operate chronically over a long period of time. These diseases are all chronic. They may be seen in an early or late phase but almost invariably the tendency for them is to progress and to become more severe. This is a basic truth which when firmly realized must strongly influence the doctor in his instruction to the patient and in his judgment as to the therapy for the condition as it presents itself before him.

By indurated leg is meant any hardness or thickening of the skin and subcutaneous tissue resulting from edema. Positive factors which influence the development of indurated leg and ultimately leg ulcer may be grouped under nine headings in this classification based on etiology: (1) postthrombophlebitic edema; (2) varicose veins; (3) obesity; (4) trauma; (5) infection (pyogenic or fungus); (6) lymphedema; (7) immersion leg; (8) arteriovenous communications; (9) systemic causes.

Usually any indurated leg has at least two and sometimes three or four of these different factors responsible for its development. Frequently trauma is an additional factor in the development of an ulcer on a leg which has

Read at the meeting of the staff of the United States Marine Hospital, Mobile, Alabama, October 24, 1947.

From the Surgical Services of Dr. Howard Mahorner, Baptist Hospital and Touro Infirmary, New Orleans, Louisiana.

long been the seat of postthrombophlebitic edema. Less often three factors such as varicose veins, obesity, trauma, and sometimes a fourth, invasion of trichophyton, are found as responsible etiologic causes in the same patient. Perhaps the most interesting of all the problems of leg ulcer and indurated leg are those in which the underlying primary cause is something far removed and of a systemic nature; for example cardiac decompensations resulting from goiter may be an incipient factor in the development of the leg condition. Often these patients are not aware that the onset of their leg trouble is so indirect.

In the management of these patients of course it is very important to have a detailed history and very carefully done physical examination, and preferably to look at the problem not once but at several different times. Often this will lead to a more accurate conclusion and thus facilitate judgment in the treatment. In selecting different measures for treating an individual case it is well to review again the different factors which are responsible for such changes in the leg. Each and every one of them should be obviated as far as possible. Sometimes an attempt to control a condition of this sort is ineffectual when the treatment is directed against the most obvious factor only, and when other causes, less obvious, but nevertheless very potent are left alone.

One ought to be well aware of the many different therapeutic measures which can be used locally, systemically, and regionally in controlling these lesions. These too may be classified under a number of different headings as follows:

1. Position—rest
   a. Elevation
   b. Intermittent recumbency; interruption of period of leg dependency
2. Local pressure
   a. Unna paste boot
   b. Compression bandages, ace type—sponges
   c. Elastic stocking
3. Local applications to ulcer
   Dyes—(2% aqueous solution gentian violet; scarlet red); zinc oxide; zinc peroxide; bismuth powder; dried red blood cells; tyrothrycin; sulfonamide crystals; sulfathiazole and urea; penicillin; streptomycin; and many other medications.
4. Temperature (optimum—neither cold nor heat; room temperature)
5. Chemical or operative interruption of the sympathetic nerve impulses resulting in vasodilatation.
6. Systemic therapy—antiluetic therapy, cardiac therapy, other drugs and operations directed to correction of a systemic factor. Systemic vasodilators tetraethylammonium chloride; ether, alcohol, tocopherol
7. Anticoagulants
   a. Dicumarol
   b. Heparin
   c. Heparin in Pitkin menstruum; leeches
8. Ligations of veins
9. Grafting of ulcers with or without excision of ulcer bed
10. Kondoleon or similar operation with or without skin grafts

When a knowledge of the range of effectiveness is considered with the factors responsible for the indurated leg the proper outline of the management of the case may become very problematic and interesting, challenging one's information, judgment, and technical ability. Certainly the treatment is something more than just dressing a leg ulcer.

TREATMENT

The treatment for indurated leg and leg ulcers can be divided into preventive and active. This involves a very broad scope, for in reality prevention of indurated leg means the prevention of anything which might create a persistent or recurrent edema of the leg. Preventive treatment includes the consideration of all approaching factors which ultimately might lead to persistent swelling of the leg including the prevention of excessive obesity, postoperative thrombosis, trauma to the leg, infection, and other such factors. The prevention of the indurated leg necessitates also the consideration of the means of removal of factors which have already been established and which created edema in the leg. It involves the knowledge of the active measures which might be employed at the time of thrombosis of the deep veins of the extremity.

The physician and patient must have the proper regard for danger signs such as edema persisting after injury from even slight trauma. If allowed to recur day after day this may result in a hard area and years later in a spreading induration with eventual ulceration whereas if it is taken care of promptly and properly with adequate rest at the time to permit the tissues to heal, the condition may subside and disappear entirely. It is well to recall that the tissue vitality of the skin varies at different

regions of the body. On the face and neck an incised wound heals very rapidly. The blood supply is good, the vitality of the skin is comparatively high and it is feasible to remove stitches early. On the other hand, on the abdomen the skin heals much less readily and stitches must be left in longer. The vitality of the skin in the region of the ankle is the lowest for any region of the body. Incised wounds heal slowly here, bruises disappear less readily, and swelling has the tendency to persist longer. It is natural for a patient to regard a furuncle of the hand and a furuncle in the region of the ankle of similar importance. Such, however, is not the case. A furuncle in the region of the malleolus particularly in an obese individual may result in a thickened, hard, subcutaneous area with spreading induration. To heal a lesion of the leg requires more time and rest with intermittent recumbency than it does to heal a similar lesion in the region of the wrist. If proper regard is not had for these physiologic facts, the patient with edema of the ankle resulting from an infection due to trauma or furunculosis may have this edema persist day after day with eventual induration of the leg in that area.

POSTTHROMBOPHLEBITIC EDEMA AND ULCER

Postthrombophlebitic edema ulcers are among the most common ones seen in private practice. Thr reason for this becomes apparent after a little study and consideration. Varicose ulcers which are also common usually can be healed by external pressure or by operation to ligate the veins. Compression bandages or elastic stockings are appliances employed successfully by patients with varicose veins and varicose ulcer. Usually the ulcer will respond to such therapy because the compression appliance not only prevents edema by pressure on the ulcer but in additon to that it compresses the varicose veins and prevents the retrograde flow of blood. In other words it improves the circulation. On the other hand, ulcer resulting from postthrombophlebitic edema is not as readily improved with external pressure. The edema there is due not to retrograde flow as in varicose veins, but it is back pressure attributable to two factors: obstructed return channels increasing the intercellular pressure and dependency of the part which adds the gravity factor to the already increased intercellular fluid. Postthrombophlebitic ulcers are usually very painful and the patients complain bitterly and suffer from them. They are not well tolerated even by indolent individuals.

The preventive treatment of postthrombophlebitic edema of course is to prevent the thrombosis. One of the most effective advances made in this regard is the employment of "early ambulation." Undoubtedly getting patients out of bed early after operation and parturition is a big help in preventing thrombosis in the veins of the lower extremity. Active movement in bed, leg exercises, are physical factors which also help to prevent thrombosis. It has long been realized that getting a patient up early after ligation of varicose veins will reduce the incidence of pulmonary embolism. Only more recently has this same trend been widely used for most other surgical operations.

Anticoagulants in the prevention and treatment of thrombosis have their advocates, and justly so. There is ample evidence reported by men who have used these drugs in large numbers of cases to show that the instance of thrombosis and pulmonary embolism is remarkably reduced by their employment (Allen, E. V.; Jorpes). These drugs are used more often as a therapeutic than as a preventive measure. Reports of their effectiveness in preventing the propagation of a thrombus and in the prevention of pulmonary embolism compares favorably with the results of surgical measures for this same purpose.

To prevent pulmonary embolism in elderly individuals preliminary deep vein ligation preceeding a major operation has been used and advocated by the Massachusetts General Hospital Group (Allen, Arthur). As a method for active treatment of thrombosis of the deep veins of the lower extremity, ligation of the femoral or iliac veins is being enthusiastically employed in some institutions and ignored in others. This measure has not been wholly accepted by the profession but it deserves a proper place. A most important consideration is whether interruption of the deep veins at

the time of thrombosis will lessen the magnitude of postthrombophlebitic edema or increase it. My experience leads me to believe that interruption of a deep vein in the thigh, never can be done with absolute impunity. There is always some residual edema from interruption of the femoral vein. This may not be apparent on restricted activity but it becomes apparent on forced activity. If a patient who has had such a ligation had to work a period of 16 or 18 hours a day, the edema would most assuredly manifest itself long before the end of the day. In reality the return circulation in an extremity in which the femoral vein has been transected is always less efficient than it is in a normal extremity. But the question as to whether operation increases or diminishes the tendency to edema after thrombosis has occurred has not been definitely determined. It possibly increases it if the thrombus is small and diminishes it if the thrombus is massive provided in each instance the thrombus is removed at the time of ligation. When there is an extensive thrombus involving a long segment of the femoral vein with massive edema of the leg, transection of the vein and removal of the thrombus with ligation may permit better development of collateral circulation during convalescence and eventually a more efficient return circulation than if the huge thrombus is left there to organize and obstruct a larger segment of the vein. My own indications for interrupting the femoral vein for thrombosis are two: when any sign of pulmonary embolism has manifested itself ligation is immediately done to prevent a major embolus; second, when there is an extensive thrombosis resulting in a massive swelling of the leg the thrombus is removed and the vein is ligated with the intention of diminishing postthrombophlebitic edema.

The active treatment for postthrombophlebitic edema is a question of much debate. It demands a selection from numerous different measures, none of which are entirely specific. The results are not uniform, sometimes surprisingly good but sometimes disheartening. This regards only the well established edema in the chronic stage following thrombosis of the deep veins of the lower extremity. It is a fact but rarely acknowledged that the return circulation of these extremities can never be expected to assume a perfectly normal capacity. In addition to this the resolution of the process involving as it does the development of collaterals and the organization and recanalization of the thrombus is one which takes a long period of time. It has been my policy to tell patients who have developed a deep vein thrombosis that it will take them a minimum period of 6 months to recover from it. This may seem like a discouraging statement to the patients, but on the other hand it gives them an understanding of the difficult problem of re-establishing circulation. The patients must be made to understand that all during this time the circulation is improving. If they make excessive demands on their circulation by keeping their legs dependent an undue number of consecutive hours the daily recurrent edema may eventually lead to an indurated leg. It is not the number of hours in twenty-four which a patient works that may precipitate induration of an edematous leg, it is the number of consecutive hours of dependency. If a patient will interrupt the period of time which he is on his feet by lying down and elevating them, part of the edema will subside and the total edema resulting at the end of the day will be less than if the whole day is spent ambulatory. It is very important for the patient to realize that "resting the leg" by putting it on another chair when he is sitting down is ineffective and almost inconsequential. The leg is still dependent. If a means of elevating the leg above the heart while he is sitting in a chair can be divised it may do some good. Otherwise he must lie down and elevate the leg above the cardiac level. During the convalescent period immediately following thrombosis it is well to advise patients to interrupt the period of dependency by mid-morning rest for a period of an hour and a mid-afternoon rest for an hour. This recumbency must be in bed and preferably part at least of that time the affected leg should be elevated. After a period of time when there is less tendency for edema they may have insignificant swelling if they rest only at the mid-day. They should continue these interrupted rest periods for 2

to 6 months. If patients carefully follow this regimen even though they have had a severe deep vein thrombosis, the residuals such as pigmentation and hardness in the region of the malleoli will be absent or minimum. In spite of this it is well to caution that if they ever get a laceration or a bruise or infection on that leg they must regard it with a certain amount of seriousness. They must respect it much more than if it occurred on the normal leg. In this way they may prevent trouble. It is much more important for them to go to bed if they have an associated factor such as laceration or bruise than it would be had this injury occurred on the opposite normal leg.

Ulcer resulting from postthrombophlebitic edema is extremely painful, and extremely disabling. If it has not been prevented and does occur, the patient will probably have to fight its recurrence even though it responds to therapy and heals promptly. He usually has to combat recurrences the rest of his life. The prevention of it, therefore, is highly important. If it has already occurred various local measures may be employed. It is my experience that ulcers in different individuals, though they all be fundamentally postthrombophlebitic ulcers, may respond with great variations to various local measures. Among the agents which might be used are the dyes including gentian violet (2% aqueous solution); scarlet red (ointment); penicillin; streptomycin; sulfonamides; urea; zinc peroxide; tyrothrycin; dried red blood cells; zinc oxide; bismuth powder; Unna paste boots and others. Almost everyone who handles these measures has a favorite. I should like to endorse dried red blood cells which at times are very effective. In addition to that the use of gentian violet in 2 per cent aqueous solution at the same time avoiding soaps and water usually works well. On the other hand it sometimes increases the dermatitis and makes the ulcer spread. Similar ulcers in different patients seem to have no unanimity of response to these local measures.

In addition chemotherapeutic agents systemically such as penicillin and sulfonamides are measures which should not be overlooked. Very frequently a period of bed rest with several spaced procaine lumbar sympathetic nerve blocks will help to reduce the edema and to obviate the pain of the ulcer and to facilitate its healing.

If postthrombophlebitic ulcers have been long standing or have recurred a number of times and if the area of induration is marked, extensive excision of this whole zone including the bed of the ulcer through the fascial layer and down to the muscles with the replacement of a split thickness skin graft has given us most gratifying results. Our experience with this type of operation has been very satisfying (Figs. 2, 3, 4). In 90 per cent of cases the patients were returned to work and have had no further trouble with ulceration in that area. The freedom from pain is a gift for which they are most appreciative. In addition the deformity resulting from excision of the area is in reality very mild. Usually after a period of time the zone is well graded with the surrounding tissues and the graft is relatively inconspicuous. It is very important to excise the entire indurated area and remove the fascial layer down to the bone or muscle. This seems to give a new base for the skin which so easily ulcerated previous to operation. Undoubtedly the deep circulation now takes care of the blood supply which was so deficient prior to the operation due to scarring. The center of the graft after operation is extremely soft for the base of it is the well vascularized underlying muscle. We usually take out a relatively wide area extending up the leg to the junction of the middle and lower third or to the middle of the leg. We have removed it over the malleoli and down to the sole of the foot. This is an operation which undoubtedly as it is better known will be more widely used for these cases. It may be employed for varicose ulcers as well as postthrombophlebitic ulcers, but it is more frequently indicated in the latter.

Just a word to warn against the ligation of superficial veins when there is a definite history of deep vein thrombosis. If compensatory varicose veins develop in a leg which has been the previous site of a deep vein thrombosis, it has been my experience that ligation of them usually does not help the return of circulation and frequently makes it worse. We have had no personal experience in the

transection of deep veins for postthrombophlebitic states as reported by Buxton and Coller. It is hard to read satisfactory results in the reports of these authors. They apparently do not enthusiastically advocate the method. A study of the type which they reported is justified in one or two large medical centers but the procedure should not be used indiscriminately and sporadically until its worth has been proved by reports from several medical centers which acclaim its value.

VARICOSE VEINS

An individual with severe or moderately severe varicose veins should be regarded as a "prestage" of indurated leg. Adequate treatment should control the retrograde flow of blood in the superficial varicose system. The comparative tourniquet test (Mahorner-Ochsner test) will usually point out the improvement to be expected prior to ligation and segmental resection. When varicose veins are operated upon, the fundamental part of the procedure is a high ligation at the fossa ovalis, resection of a small section of the saphenous vein and separate transection and ligation of the adjacent tributaries. In addition to this, if the comparative tourniquet test shows incompetence of the valves of the veins communicating between the deep and superficial systems below that level, additional ligations or segmental resections should be done to control most of this back flow. In considering this operation in the light of an indurated leg it may be regarded as preventive surgery. In reality of course there may be other indications for the ligation.

Usually the onset of induration of the leg in a patient with varicose veins is manifested by thrombosis of a small vein in and around the malleolus at the lower end of the saphenous system. In that area edema and hardness appear. The area may become discolored and even pigmented. It may be tender. This should be regarded as a danger phase. External compression and interval rest in the middle of the day will probably help to restrict the spread of induration. If the patient ignores these signs staying ambulatory many hours a day, the swelling may recur daily and subcutaneous tissue may become hard in that area. Eventually fibrosis and scarring with persistent dermatitis, scaliness, and weeping of the skin may result in an ulcer.

When this stage presents itself it is imperative that the varicose veins be ligated in order to improve the circulation and to stop the retrograde flow (Fig. 1). Even if ulceration has supervened, ligation becomes a basis for therapy. As long as the circulation is impaired with chronic passive congestion of the tissues the pathologic process will progress. Local applications to the ulcer are of much less fundamental importance in the average case. However, if a patient has any condition which precludes the advisability of surgery, the compression therapy with elastic stocking or temporary Unna paste boot may be accepted. Severe varicose ulcers with induration which persist after ligations should be excised and the area grafted with skin (Fig. 2).

Unless small intracutaneous varicose veins without large ropy varicosities have developed a complication such as thrombosis, ligation will probably not improve them sufficiently to justify its being done purely for a cosmetic reason. This statement, of course, is made in respect to a lower extremity which is the seat of the varicose veins of the small intracutaneous telangiectatic variety only. When they are large, dilated saphenous veins or other trunks with marked ectasia the improvement in the circulation may be marked following ligation. Moreover small superficial intracutaneous varicose veins will not respond properly to injections of sclerosing solution. Usually the patient with these is seeking cosmetic improvement. If they are injected with a sclerosing solution, it is true the small varicosity may disappear. On the other hand there will be a discolored area leaving a spot which is as cosmetically imperfect as the varicosity. It is my policy to advise patients with small varicosities, who are seeking cosmetic improvement only, to let their veins alone.

When varicose veins are moderately severe or severe, ligation at the proper level is the treatment of choice. Then improvement in circulation efficiency may be expected. Either varicose veins are severe enough to justify ligation or they are mild and should be left untreated because they cannot be improved

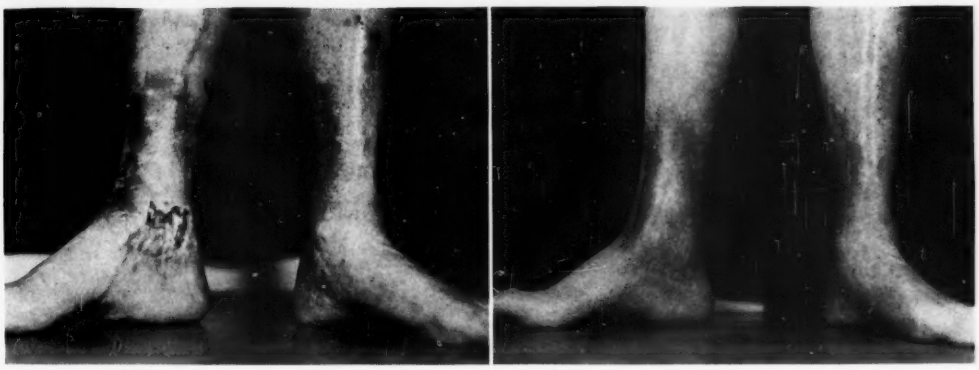


Fig. 1. Varicose ulcer before and after ligation of the saphenous veins. The ulcer healed promptly after the ligation. It had been present almost continuously for some 12 years prior to ligation.

cosmetically. If they progress and become more severe, ligation can be done at a future date. It seems always fair and even important to tell the patient that whereas varicose veins can be improved by ligation, the tendency to develop varicose veins cannot thus be removed. Patients with obesity and superficial varicose veins should be warned against striking their limbs against chairs or other objects. In addition, if they have even a minor injury resulting in thrombosis, they should be carefully cautioned to interrupt the period of dependency of their legs and elevate them for an hour or more during the middle of the day until the swelling disappears. Compression therapy in the form of a semielastic bandage (elastoplast or ace bandage) at this period is frequently very helpful. If varicose veins are present and if thrombosis occurs in the varicosities the thrombosis is an additional indication for surgery. When ligations at the proper sites are done for the varicose veins after thrombosis occurs in the varicosities the dual effects of the operation are subsidence of the thrombosis and improvement of the varicosities.

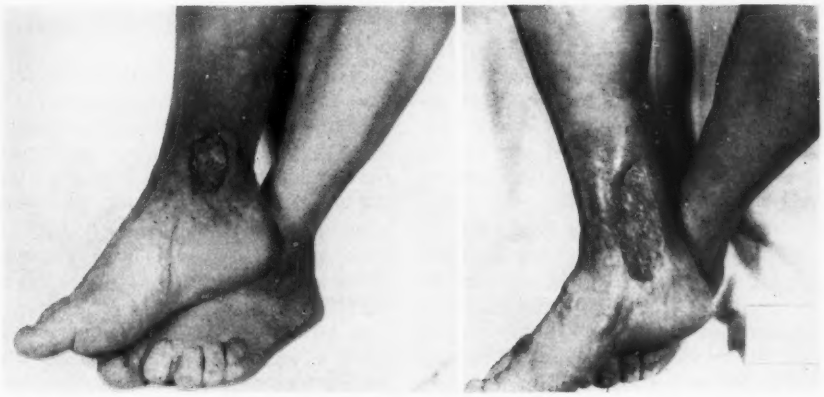


Fig. 2. Varicose ulcer before and after excision and skin graft. The patient's varicose veins had previously been ligated but prior to ligation the indurated area had been present so long and so much scarring was present that she was not able to prevent the skin from repeatedly breaking open and ulcerating. Following excision and skin graft she has remained well for over 1 year in spite of the fact that she is very active.

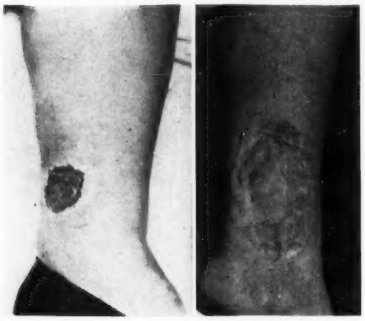


Fig. 3. An ulcer of the leg before and after excision and skin graft. The main etiologic factors here were obesity and trauma. She previously had minor intracutaneous varicose veins injected. The ulcer had been present for a period of 5 years. After excision of the indurated area down through the fascial layer and application of the split thickness skin graft this patient has remained well. She is very active. The center of the grafted area is quite soft since underlying the skin there is muscle. This affords good vascularity in the surrounding area.

OBESITY

Obesity is a frequent factor in the development of indurated leg (Fig. 3). It is rarely of itself the only factor. Combined with trauma, thrombosis, infection, lymph stasis, or systemic causes of passive congestion such as cardiac disease, it may exert its effect in such a manner as to increase edema and bring about fibrosis of the subcutaneous tissue. Patients who are obese have a tendency to thrombosis. If they have varicose veins, they should be cautioned about the dangers of even slight trauma which might precipitate a thrombosis and lead to induration. In addition localized infections such as furuncles on the lower extremity in the obese patient should be respected as conditions much more likely to lead to chronic trouble than if the same process occurred in a patient of normal weight. Once established erysipeloid with its recurrent infection and high fever has a fertile soil in the obese leg. These repeated infections lead to chronic swelling and eventually to thickening of the subcutaneous tissue.

The preventive treatment of indurated leg as far as this factor is concerned involves the prevention of obesity with all of its difficulties. In addition to that it involves the prevention of other associated factors such as injury or long continued dependency which might increase the tendency of the intracellular fluid to become static and pool in and around an obese ankle. Whenever an obese patient develops the slightest additional complication, such as a small thrombosis in the vein of a lower extremity, he should be cautioned to treat the condition as if it were something potentially very serious. Compression therapy and bed rest may help it to resolve and prevent it from becoming chronic.

TRAUMA

Trauma may be the incipient cause of indurated legs in several different ways (Fig. 4). Even slight blows to the subcutaneous tissue particularly around the internal malleolus may result in edema. Apparently at times this edema of the subcutaneous tissue and overlying skin is not attended by any thrombosis in the veins. There is undoubtedly a vascular disturbance which may be so severe that vasospasm of the veins and arteries of that extremity is a decided factor in the persistence of edema.

One frequently hears the story of a patient aged 50 that some 15 or 20 years ago struck his leg on a sharp corner of a rocker. It hurt and was annoying at the time but the patient was very busy and had to continue working for many hours a day. The swelling continued day after day. He felt that it should disappear spontaneously. Perhaps he did not even go to a physician, but if he did he probably did not foresee the ultimate end-result, namely an indurated leg and ulcer. To prevent induration of the leg from such causes the patient should respect the possibility that the effects of the injury may become chronic. He should rest in the middle of the day with the leg elevated and should use compression bandages of the ace type, or if the trauma has been severe enough he should remain recumbent most of the time for a period of a few days.

Another type of trauma which results sometimes in an indurated leg is that from a more severe injury such as a fractured femur or a fracture of the tibia. Hardness and induration of the subcutaneous tissue around the malleoli are commonly seen as sequelae of these injuries. There are probably two different pathogenic

onsets for induration resulting from such trauma. One is that which accrues from injury to the deep vein with thrombosis at the time of the fracture. Because the patient was lying in the bed with the limb elevated the immediate consequences of this thrombosis of a large collecting vein may have been overshadowed by the objective evidence of the fracture itself. Only in the convalescent period after union, when the patient was becoming rehabilitated was it noticed that the leg swelled inordinately.

Injury to the lymphatics and smaller veins in the region of the ankle attending the fracture of the tibia may cause considerable chronic disturbance in the circulation and tendency to subcutaneous edema persisting long into the convalescent period. Interrupted dependency and external compression bandage during this phase is very very important. All of these injuries are attended with vascular disturbances with vasospasm. Even minor injuries may have a posttraumatic syndrome equivalent to Sudeck's atrophy with edema and eventually with atrophy of bone and persistence of the pain.

The active treatment of the edema which results from trauma is rest and elevation either constant or interrupted, whichever may be necessary. As a supplementary measure external compression is very valuable. Sometimes temporary interruption of the sympathetic nervous impulses by procaine lumbar sympathetic nerve blocks is of great value. Careful judgment should be used in selecting different measures but in all instances great respect should be exercised when edema is occurring day after day. If it does so and does not abate, indurated leg is inevitable.

INFECTION

Infection has been mentioned a number of times as a partial factor operating with other factors in the production of indurated leg. One should recall to mind the tissue vitality of the skin of the leg. It is relatively very poor. Any infection there resulting from an open wound or furuncle is apt to heal very slowly. Resolution takes much more time, and an important part of the preventive and active treatment of such lesions is to regard them as being potentially more dangerous and more likely to develop into chronic stages than are similar lesions elsewhere on the skin of the body.

Fig. 4. The resultant of excision and skin graft of an ulcer of the leg which according to the history followed a bruise to the leg in the region of the ankle. Apparently trauma had been a major factor in this ulceration. No preoperative photograph is available, but the ulceration was severe and it had been present for a period of a year. It was extremely painful. This patient, aged 36 years, is an active business woman. Since her graft in July 1946, she has remained well.

Infection in the skin in the form of a recurrent erysipeloid or erysiepelas is an extremely dangerous, extremely disabling illness. The attacks tend to recur after a period in which the host has been very active. Practically all of the attacks begin at one spot. The patient describes an itching sensation and then usually an onset of a chill with high fever. Within a few hours the leg is intensely red and very painful and the patient is extremely sick. The repetition of the infection over and over again results ultimately in much hardness of the leg, skin, and subcutaneous tissue and sometimes in ulceration. We have used sulfonamides, penicillin, and other measures, in an effort to prevent the attacks. None of these measures have worked entirely satisfactorily. In one instance in a young man who was having recurrent attacks of erysipeloid I excised the trigger area. We studied carefully the onset of the trouble. Each attack seemed to begin around the malleolus. The following is his history:

M. S., a young man, aged 19 years, came under our care on August 2, 1946. For 6 years he had attacks of chills and fever accompanying a painful swelling of the left foot and leg. The last attack had

Fig. 5. Congenital lymphedema in a 2 year old child. There is puffiness in the dorsum of the left foot and slight increase in size of the left leg to the middle of the calf. The subcutaneous tissue on the dorsum of the left foot including the fascia was excised through an "inverted-staple" shaped incision. This patient disabled prior to operation has been observed now for a period of 5 years. The result is excellent. A slight thickening of the left leg persists. Since congenital lymphedema often leads subsequently to attacks of erysipeloid, conditions such as this should be treated surgically early in life. The photographs show the legs preoperatively and 20 months after operation. (In January, 1948 this patient, now aged 9 years, had a first attack of erysipeloid induced by epidermophytosis.)

been in June 1946. The condition looked all together like a recurrent erysipeloid. Examination at the time he was first seen revealed negative findings except for slight thickening of the subcutaneous tissue in the lower half of the left leg from the calf to the ankle. He was asked at this time just where the first signs of the infection appeared. He was not certain but he thought that the attacks began in the region of the ankle. He was sent home, advised to take 300,000 unit doses of penicillin once a week for a period of 6 weeks. On December 14, 1946, he returned again from his home in another state. He had had additional attacks. At this time it was observed by him in the recent attacks that they always began in the region of the internal malleolus.

It was decided then to excise an area of skin, subcutaneous tissue, and fascia; the zone in which the attacks were thought to begin. On December 14, 1946, this was done. A split thickness skin graft was obtained from the right thigh and was placed on the denuded area. In addition, in order to improve the circulation to the lower extremity, a left lumbar sympathectomy was performed December 20, 1946. A report from this patient received in November 1947 states that he has had no attack of erysipeloid since the operation except a very mild one in September 1947 which was initiated after excessive exercise. He attends a university and states that he is able to lead an active life.

We felt that the etiology of this man's condition was an acquired lymphedema. Whether the lymphedema followed the erysipeloid or whether it was a primary factor with a superimposed recurrent infection we were not able to determine from the history. There is no familial history of lymphedema in his case.

In addition to the bacterial types of infection which may be factors in the development of the indurated leg, one should consider trichophytosis as a common secondary invader to a chronically edematous skin. It is not easy to prove this each time by laboratory methods. On the other hand it has been proved that fungus of this type may affect the skin. It usually does so in the region of the internal malleolus. It is necessary to combat onychomycosis and trichophytosis of the feet in patients with recurrent or persistent swelling of the leg and with a scaly dermatitis of the malleolar region. In a very warm climate one gains the impression that this fungus is very widespread and very common. It is abetted by moisture, and in its presence soaps and water seem to enhance the pathologic process. Apparently at times the fungus infection of the trichophyton variety may be the initial and only cause of the leg ulcer. It is true that without other complications this lesion may fall into the category of dermatology, but one handling leg ulcers cannot help being impressed with fungus invasion as a factor in the development of leg ulcers.

LYMPHEDEMA

Lymphedema may be familial or it may be sporadic, it may be acquired later in life or it may be congenital. If it is seen early in life and there is a family history of it, it may be termed Milroy's disease or Nonne-Milroy disease. If there is a family history of it and if it presents itself at puberty it may be regarded Meige's disease. Moreover it may be secondary; the result of obstruction of major lymphatic channels from repeated infection or by parasitic invasion, namely filaria.

The condition may be a diffuse thickening of the subcutaneous tissue of the leg or it may be localized subcutaneous deposit with ectatic lymphatics, fat, and fibrosis. If it is observed early in life the tendency for it is to advance, spread, and become more severe as the child grows older. Many of these patients have

very little trouble from it. It is much more common than is usually appreciated and without complications it may interfere little with a very active life. On the other hand it is fertile soil for infections.

Measures to prevent a leg which is the seat of lymphedema from becoming indurated involves an effort to avoid all associated factors. When any complications appear they should be treated cautiously and with full knowledge that they may change the process into one which could be very disabling. Should induration and ulceration appear the active treatment may mean excision by a Kondoleon type of operation. Even before ulceration excision particularly of localized lymphedematous masses may be indicated.

I believe that when localized sporadic lymphedema is present and seen early in life it should be excised. The following is a brief abstract of such a case.

The child (F.P.), aged 2 years, when first seen had a marked swelling on the dorsum of the left foot. It had been present since birth. The swelling seemed to be increasing in size and because of it a shoe could not be worn on that foot. The swelling was soft, was never painful.

When examined the patient showed a diffuse soft swelling of the foot involving the dorsum and extending to the ankle. It was about 2 centimeters thick in its greatest depth and was about 6 by 6 centimeters in the other dimensions. In addition to that the left leg was slightly larger in circumference than the right. The subcutaneous tissue was thicker than normal but not hard. The condition was regarded as congenital lymphedema. The child was kept under observation for 1 year. Then an operation was performed.

Through a horseshoe incision elevating the skin the whole zone of thickened subcutaneous tissue was excised, including the fascia. The skin was then replaced. The wound healed promptly and the child has made an uneventful recovery. She has developed normally. She has been observed at intervals for 5 years since the operation. The result is excellent (Fig. 5). Pathologic examination of the section removed revealed fat, dilated lymphatic spaces and fibrous tissue.

The onset of recurrent erysipelas in a patient with lymphedema of the lower extremity leads to a very serious point in judgment. When lymphedema is severe a Kondoleon type of operation may be of great advantage in relieving the enormous swelling. If the trigger zone could be excised at the same time the recurrence of the attacks may be obviated. I believe that if these patients can be seen soon after the onset of recurrent erysipelas, some effort should be made to excise the zone in which the infection lies dormant during remissions. We have tried giving patients various chemotherapeutic measures to reduce the number of attacks or to obviate them. Usually it is not successful, but in a few instances we have seen apparently what amounts to a cure, that is cessation of the attacks of infection in the leg with fever. I have seen patients who I thought were better off to have an amputation because of continued disability from recurrent erysipelas than to try to keep the lower extremity. Usually when told this, they are very reluctant even though they have spent many months out of the last year convalescing from an attack.

Fig. 6. Immersion leg. Chronic swelling and thickening of the subcutaneous tissue with ulceration of the leg which was initiated after this officer had to lie immersed in water for a period of 36 hours during an invasion. This condition was treated conservatively mainly by restricted activity. Since returning to civil life, he had been very active and consequently had daily recurring edema of the lower extremities. Impaired circulation such as this will not withstand many consecutive hours of dependency.

IMMERSION LEG

The name immersion leg is intended to designate chronic edema of the leg which results after the trunk or lower extremities have been immersed in water for many hours or days. This injury resulted many times during war when boats were torpedoed and survivors were picked up after they had been immersed in

Fig. 7.

Fig. 8.

Fig. 7. Leg ulcer, partially the result of an indirect (systemic) cause. The patient, aged 25 years, had a funnel chest with displacement of his heart and interference with his return circulation resulting in chronic edema of the legs which he says was present prior to the ulceration.

Fig. 8. Postoperative views of patient shown in Figure 7. He "felt better than he ever had before" and now weighs 10 pounds more than he ever weighed before. The ulcers present on each leg have healed and have recurred since the operation.

water for many hours. The following brief history is typical of these cases.

Captain H., aged 47 years, was in the invasion of the Philippines. His company was "pinned down" by the enemy. For 36 hours he was lying half in the water and half out. The temperature at the time was moderate. Ever since then his legs have been swelling. After his return to civil life he has assumed his old job as harbor pilot. This requires him to work many hours a day on some shifts and when he does so the swelling is pronounced. Recently an ulcer had appeared near the external malleolus of the right leg. Examination revealed tremendous swelling and induration of both legs below the middle of the thighs (Fig. 6). A small leg ulcer was present near the right external malleolus. Thorough investigation revealed that he did not have filariasis. A scaly dermatitis was found on both legs above the ankles suggesting a fungus infestation of the skin, a condition he, himself, termed "jungle rot." The treatment advocated was conservative with more restriction of activity.

The cause of recurrent edema after immersion in water is obscure. Apparently the vessels lose their tone and the tissues are damaged so that intercellular spaces remain open and subject to ready filling.

ARTERIOVENOUS COMMUNICATIONS

Any condition in which the arterial blood is emptied directly into the larger veins may lead to edema and eventually to induration and ulceration. Arteriovenous communications are mentioned to make the classification comprehensive. If the lesion is congenital or occurs early in life from trauma, the lower extremity is likely to be longer and larger than the opposite. The diagnosis when an arteriovenous communication is large enough to result in edema should be more or less obvious. If induration alone is the symptom presented, diagnosis of arteriovenous communication will not be overlooked if it is remembered as a possible cause. The proper treatment is surgical attack on the arteriovenous communication.

SYSTEMIC CAUSES

It is surprising sometimes to find the cause of an indurated leg far removed anatomically and even physiologically. I have seen a patient whose chief complaint was indurated leg and leg ulcer, and the fundamental cause behind this predominant problem was a nodular goiter whth hyperthyroidism. The patient had been having mild cardiac decompensation with edema of the legs. The edema had resulted in induration in the region of the internal malleolus and ulceration supervened. Even more interesting was a patient sent because of leg ulcers. His history is as follows:

J. M., aged 25 years, developed an ulcer on the right leg 10 years ago. Several injections were given in the veins and the ulcer healed. Since that time ulcers have developed on both legs in the region of both the internal and external malleoli. His legs swell almost daily. From birth he had a marked depression in the center of his chest.

Examination revealed a tall young looking man. He had a most pronounced funnel chest. There was extreme depression of the sternum at the lower end. In addition to this he had leg ulcers on both legs near the internal malleoli and pigmented indurated areas near the external malleoli which had been previous sites of ulceration (Fig. 7). Careful studies were done on this patient which will not be reported in detail here. We estimated that his circulation was deficient, partially due to the marked displacement of his heart to the left and possibly also due to pressure on the inferior vena cava by the retrodisplacement of the lower end of the sternum. On July 2, 1947, he was operated on for the funnel chest. The lower portion of the sternum was removed and after reshaping it, it was replaced so that the defect was obviated. During his convalescence there was considerable drainage from the wound and infection supervened. We thought it was necessary to take out the graft which consisted of the lower end of the sternum and the adjacent cartilages. The wound healed. The ulcers in the meantime healed entirely. He was seen again in January 1948. The circulatory efficiency had improved remarkably. He weighed 10 pounds more than his previous maximum weight (Fig. 8). He felt "better than he had ever felt." His venous pressures were lower than preoperative levels and were identical in leg and arm veins. Prior to operation the pressure in the leg veins at cardiac level was higher than that of the arm veins. The ulcers had healed following operation and ankle edema had disappeared. In January 1948 he had a recurrence of 2 ulcers on the right foot and ankle which appeared to be due to trichophyton. Edema of that ankle only was noted at that time.

Various other distant causes may be factors in the production of induration and ulceration

Fig. 9. Severe ulceration and induration of the leg. This is a neglected case of leg ulcer which has multiple causal factors including varicose veins and obesity. The subcutaneous tissue is thickened and very hard. Amputation is among the measures to be seriously considered for this degree of disability.

of the leg by interference with return circulation. For example, cirrhosis and ascites, and pelvic tumors which press on the iliac veins may initiate chronic passive congestion. In addition to this systemic factors such as diabetes and arteriosclerosis may be casual components in the development of leg ulcer and induration. These lesions rarely are the sole cause of leg ulcers but they may be a contributing cause and in order to heal the ulcer and prevent its recurrence all factors should be obviated as far as possible. Sickle cell anemia may be responsible for leg ulcer. Usually in this and some other systemic condition such as tuberculosis, ulceration appears first and induration is a secondary accompaniment. Syphilis is frequently a cause of leg ulcer and if it persists over a long period of time marked induration may result. Filariasis is a systemic parasitic infestation with localized lymphatic obstruction is not to be forgotten as a possible cause of acquired lymphedema.

SUMMARY

A clinical viewpoint involving the classification of indurated leg and leg ulcers based on the etiology is given. These conditions should be regarded as chronic progressive processes. Various factors are usually responsible for any induration of the leg and leg ulcer. It is im-

portant in the management of these conditions to attempt to obviate each and every factor. The treatment is preventive and active. Preventive treatment usually involves a respect for the seriousness of daily recurring edema of the leg. Various measures to be used in prevention and active treatment were mentioned. Some indications as to judgment and selection of different measures were discussed. Emphasis was repeatedly placed on the importance of preventing the recurrence of swelling in the leg day after day. This is a predisposing factor to indurated leg and the patient should be warned of its potential seriousness.

A great deal can be done not only to prevent these conditions but also to control them and at times to cure them. Several individual cases were cited to illustrate the selection of surgical measures for some of these problems.

If a patient is entirely incapacitated because of an indurated and ulcerated leg and if the prospect of cure of the ulcer is poor, amputation should be considered. Usually patients are repelled by such a suggestion but the truth of the matter is that they would be better off living without a leg than living only for it.

REFERENCES

1. Allen, Arthur W. Surg. Gyn. Obst., 1947, 84:-519.
2. Allen, Edgar V. J. Am. M. Ass., 1947, 134: 323.
3. Buxton, Robert W., and Coller, Frederick A. Surgery, 1945, 18: 663.
4. Homans, John. Surg. Gyn. Obst., 1944, 79: 70.
5. Jorpes, J. Erik. Surg. Gyn. Obst., 1947, 84: 677.
6. Mahorner, Howard, and Ochsner, A. Ann. Surg., 1938, 107: 927.
7. Meige, Henry. Presse méd., 1938, 2: 341.
8. Milroy, W. F. N. York M.J., 1892, 56: 505.
9. Morton, John J., Mahoney E. B., and Mider, G. B. Ann. Surg., 1947, 125: 590.
10. Nonne, M. Arch. anat. physiol., Leipzig, 1891, 125: 189.

EDITORIAL

SURGERY
Gynecology and Obstetrics

FRANKLIN H. MARTIN
Founder and Managing Editor
1905–1935

LOYAL DAVIS, Editor

Associate Editors
SUMNER L. KOCH MICHAEL L. MASON
M. E. SPENCER, Assistant Editor
JAMES T. PRIESTLEY, Associate, Editorial Staff

JANUARY, 1949

BRONCHIOGENIC CARCINOMA

WITHIN a period of 35 years primary carcinoma of the lung has advanced from a position of obscurity as a rare curiosity to one of great frequency. There is even some evidence now to indicate that it has displaced carcinoma of the stomach as the most common visceral cancer. Statistical studies at the St. Louis City Hospital and at the Charity Hospital in New Orleans (Ochsner and DeBakey[1]) have shown that actually primary carcinoma of the lung is more frequent than that of the stomach. This finding is of particular significance because these hospitals represent a cross section of the population of those two cities, although at a lower economic level.

Because of its frequency it is important that great emphasis be placed on the desirability of early diagnosis and on the now well established fact that it is no longer an incurable or hopeless condition if the proper treatment is instituted at a sufficiently early time.

In regard to the diagnosis certain points should be stressed. It is primarily a disease of males (about 6 males to 1 female) during or after middle age. Since primary cancer of the lung practically always, if not always, arises in a bronchus, the most common symptom is cough. In more than half of the cases the sputum sooner or later becomes characterized by streaks of blood. These two features are more pronounced if the cancer has arisen in a major bronchus. Unfortunately when it arises in a small bronchus at some distance from the main stem bronchus of either the lung or of any of the lobes, both cough and bloody sputum may be absent. Such patients often have no warning of symptoms until the condition is too far advanced to be curable. As in other forms of cancer, pain and loss of weight are usually late symptoms and often denote incurability. It cannot be stressed too emphatically that a middle-aged man with an unexplained cough and bloodstreaked sputum should be strongly suspected of having a bronchiogenic carcinoma and that steps should be undertaken at once to make the appropriate examinations.

Of the methods of examination the most important are the x-ray, bronchoscopy, and the newer procedure of examining the sputum or bronchial secretions for cancer cells.[2] Even with a combination of these methods a definite diagnosis can be made in only about 85 per cent of cases. In the remaining 15 per cent it is necessary to perform an exploratory operation. Experience has shown, however, that in practically 100 per cent of cases when both the history and examinations are suspicious

[1]Ochsner, A., and DeBakey, M. Surgery 1940, 8:992.

[2]Wandall, Hans. Study on Neoplastic Cells in Sputum. Copenhagen: Arnold Busck, 1944.

the tentative diagnosis of bronchiogenic carcinoma is found to be correct at the exploratory operation. It is dangerous in such cases to subject the patient to a period of observation, waiting for the diagnosis to be established. Many curable cases are converted into incurable ones by such a procedure.

There was no successful treatment of this condition until 1933.[1] In April of that year the author of this editorial had the opportunity of performing the first successful one-stage removal of a lung in a patient who had a squamous cell bronchiogenic carcinoma arising in the main bronchus of the left upper lobe. The patient is still living and well more than fifteen years later. Since that time the operation of total pneumonectomy has become the standard treatment for bronchiogenic carcinoma throughout the world. This procedure follows the rule of the surgical treatment of cancer of other organs in that a higher percentage of 5 year cures can be obtained if the whole organ rather than only a part is removed. It has the additional advantage over a mere lobectomy in that it makes possible the removal of more regional lymphatics.

During the fifteen years that have elapsed since the first successful one-stage pneumonectomy much has been learned about the curability of this otherwise hopeless condition as well as the limitations of the operation. Also of course the technical aspects of the procedure have been greatly improved (Rienhoff[2] and Crafoord[3]). Likewise, as experience has accumulated, much has been learned also about bronchiogenic carcinoma itself, although the etiological factors and why the condition is chiefly one of the male sex remain obscure.[4,5]

[1]Graham, E. A., and Singer J. J. Am. M. Ass., 1933, 101: 1371.
[2]Rienhoff, W. F., Jr. Bull. Johns Hopkins Hosp., 1933, 53: 390.
[3]Crafoord, C. On the Technique of Pneumonectomy in Man. Stockholm: Tryckeri aktibolaget Thule, 1938.
[4]Graham, E. A., and Womack, N. A. J. Thor. Surg., 1945, 14: 106.
[5]Graham, E. A. Ann. Roy. Coll. Surg., England, 1947, 1: 248.

Our own experience at the Barnes Hospital is based on a series of 1117 cases of proven bronchiogenic carcinoma from July 1, 1920, up to July 1, 1948. Since the first case of successful one-stage pneumonectomy on April 5, 1933, we have performed 296 operations of that sort, of which 184 have been for malignant tumors. One of the most distressing features of the problem is the relatively small number of patients who present themselves with a cancer early enough to permit the removal of the lung. In our cases only about 25 per cent have had a pneumonectomy. We have probably been more conservative in this respect than some other surgeons. Space is too limited to permit here a discussion of this point except to say that we have not been convinced of the wisdom of going ahead with the removal of the lung when it is obvious that cancer tissue will be left behind. The chief deterrent factor, however, is usually the finding, in those patients in whom exploratory operation has been done, of invasion of the hilar vessels by the cancer, a condition which would make the operation not only excessively dangerous but futile as well. In a recent series of 260 cases we performed a pneumonectomy in 22.3 per cent. In an additional 32 per cent we carried out an exploratory operation but found the cancer too far advanced in our opinion for a resection of the lung. In the remaining approximately 45 per cent an operation was not performed because either the condition was obviously hopeless or other features seemed to preclude the chance of a successful operation, such as advanced age or general poor condition.

Two questions of paramount importance are, of course, the immediate operative risk and the chance of a five year cure. It is gratifying that the operative mortality has steadily declined until now it is very respectable. In the early years it was 53 per cent, but last

year (1947) of 39 pneumonectomies for cancer we had only 2 deaths, a hospital mortality therefore of only 5.1 per cent. Those who are more radical in their attempts at resection will have a higher operative mortality.

As regards late results there is reason to be optimistic. Of our own series of 53 patients who had pneumonectomies prior to 1942, 15 are alive and well. This is a five year survival rate of 28 per cent. The next five year period will undoubtedly show better results because of the sharp reduction in operative mortality. After all, in the early years 53 per cent or 28 patients died of the operation and there was no chance therefore to determine how many of that number might have lived more than 5 years if they had survived the operation. This is to be contrasted with the present operative mortality of 5 per cent. Of the five year survivors in our series the highest percentage was in the malignant mixed tumors (57 per cent of 16 patients). In 22 cases of squamous carcinoma 3 patients (14 per cent) are alive 5 years later; and in 15 cases of undifferentiated carcinoma 3 patients (20 per cent) are alive after 5 years. In those cases with invaded lymph nodes naturally the results are not so good. Yet some are still living. Of 5 patients who had pneumonectomies for malignant mixed tumor with node invasion 2 are alive more than 5 years as is 1 patient of 12 with squamous carcinoma and lymph node invasion. Obviously, as is true with cancer in general, the earlier the lesion the better the result, but involvement of regional lymph nodes does not make the prognosis completely bad.

In summary, one may say that bronchiogenic carcinoma is now recognized to be one of the most frequent forms of cancer. The operation of total pneumonectomy offers hope to those victims of this disease who prior to 1933 had no hope. Nowadays the principal problem in improving the results is to have patients come for help early enough to permit the operation. This means education of the profession to the recognition of the frequency of this condition, the necessity of early examinations of a proper kind, and the fact that the early case is curable.

EVARTS A. GRAHAM

MEDIASTINAL TUMORS

MEDIASTINAL tumors are relatively rare lesions. It is safe to predict, however, that the practice of making routine roentgenologic examination of the chest will establish the fact that mediastinal neoplasms are much more common than past experience would indicate. Bronchiogenic carcinoma was regarded as a rare disease years ago but it is now known to be one of the most common forms of cancer. These facts suggest that other intrathoracic tumors may be of more importance than has been attributed to them in the past.

Accumulated data from Army experiences during the past war are not yet available. It is significant, however, that 109 patients were operated upon for mediastinal tumors at Army thoracic surgery centers in the United States during a period of approximately three years. This series did not include cases of mediastinal neoplasms of lymphatic origin, such as lymphosarcoma, mediastinal Hodgkin's disease, and similar conditions. It is of particular significance that in 94 of the 109 cases no clinical manifestations of intrathoracic disease were present; the tumor was found on routine roentgenographic examination.

Successful treatment of mediastinal tumors depends on their detection before clinical signs are apparent. Block excision as used in carcinoma of the breast, skin, and elsewhere is precluded because of the anatomic arrangement of the mediastinum. Successful surgical

therapy, therefore, is impossible unless the lesion is localized and encapsulated.

In the past there was a tendency to "watch" asymptomatic mediastinal masses. This policy for intrathoracic tumors was understandable when the risk of exploratory thoracotomy was considerable. It can be stated categorically, however, that at the present time the danger of exploration of the mediastinum is trivial provided the patient is in reasonably good condition and provided qualified anesthetologists and surgeons are available.

The discovery of a mediastinal mass by routine roentgenologic examination, with or without associated clinical manifestations, demands positive diagnosis. Should no available diagnostic procedure provide an infallible method to determine preoperatively the exact nature of a mediastinal tumor, only two therapeutic methods are available: radiation therapy and surgical extirpation. With few exceptions the only mediastinal tumor which will respond to radiation therapy is one of lymphatic origin (lymphosarcoma, Hodgkin's disease, and others.)

Radiologists and surgeons experienced in thoracic disease should be able to predict, in the majority of cases, from roentgenographic and clinical evidence the presence of a lymphoma. These tumors have a tendency to produce clinical symptoms early and their appearance on the roentgenogram is rather characteristic. Properly employed radiation therapy is invaluable both as a therapeutic and diagnostic measure if a tumor of lymphatic origin is suspected. Disaster may be anticipated however, if injudicious radiation is employed in all cases of mediastinal tumors.

The mediastinum may harbor almost any type of tumor. For practical purposes it is convenient to classify common mediastinal tumors in two varieties: anterior mediastinal tumors and posterior mediastinal tumors.

The most common anterior mediastinal tumor is a neoplasm of lymphatic origin. Lymphosarcomas, Hodgkin's disease, granulomas, and other lymphatic tumors usually have a characteristic pattern which would indicate the administration of a test dose of radiation therapy. It should be emphasized however, that about one third of the malignant lymphomas are slow in their reaction to radiation. If after a period of approximately one month of adequate radiation therapy, there is no change, thoracic exploration should be performed to determine the exact nature of the lesion.

Dermoid cysts and teratomas of the mediastinum are the second most common neoplasms situated in the anterior mediastinum. In discussing these neoplasms Harrington [1], [2] simplified the terminology by employing the inclusive term "teratoid tumors."

The chief source of confusions in the diagnosis of anterior mediastinal tumors is the differentiation between lymphatic tumors, teratoid tumors, thymomas and bronchiogenic cysts. When academic pride is excluded there remains only the choice between the lymphoma group and all the others. If any doubt exists thoracic exploration should be performed to establish a positive diagnosis.

Posterior mediastinal tumors are chiefly of one common variety. Neoplasms of neurogenic origin are by far the most common. Kent[3] and his co-workers collected 105 cases in the medical literature; 29 cases were recorded in my Army experience.[4]

The incidence of primary nerve tumors of the mediastinum is unknown. Most of these lesions are found on routine roentgenologic examination and are asymptomatic. Occasionally, nerve involvement may cause pain; if

[1]Harrington, S. W. Arch. Surg., 1929, 19: 1687.
[2]Harrington, S. W. J. Thoracic Surg., 1933, 3: 50.
[3]Kent, E. M., Blades, Brian, Valle. A. R., and Graham, E. A. J. Thoracic Surg. 1944, 13: 116-161.
[4]Blades, Brian. Ann. Surg., 1946, 123: 749.

the sympathetic chain is involved Horner's syndrome may be evident. Too often, however, definite clinical signs of disease indicate the presence of malignant degeneration and inoperability.

Once considered rare bronchiogenic cysts are now known to be fairly common. Laipply[1] reported 35 cases in 1945. In a period of three years, 23 mediastinal bronchogenic cysts were removed in Army hospitals. These cases were all found on routine x-ray examination. Pericardial cysts may occur. Thymomas are relatively rare. These tumors are usually located in the anterior mediastinum in a substernal position. However, bronchogenic cysts, lymphomas and thymomas may occur in either the anterior or posterior position.

Other varieties of mediastinal tumors include fibromas (probably neurofibromas), tumors of thyroid origin, tuberculomas, cysts of the esophagus, osteochondromas, and other unusual neoplasms. Enlarged lymph nodes, Boeck's sarcoid, and aneurysms can be mistaken for mediastinal tumors.

Until precise diagnostic methods are available, therapeutic measures in the treatment of mediastinal tumors will remain limited to radiation therapy and surgical removal. Tumors which respond to roentgen therapy are usually incurable; others may be amenable to surgical extirpation.

The choice between radiation therapy and surgical intervention will depend, first, upon the tentative diagnosis and, second, upon the danger of exploratory thoracotomy. If roentgenologic and clinical evidence indicate the presence of a lymphoma a test dose of radiation should be given. If improvement does not follow in due course, thoracic exploration should be carried out unless the general condition of the patient precludes the use of any type of surgical intervention.

BRIAN BLADES.

[1]Laipply, T. C. Arch. Path., 1945. 19: 153–161.

THE SURGEON'S LIBRARY

THE BOOK SHELF

JOHN COAKLEY LETTSOM AND HIS LITERARY FRIENDS

JOSIAH C. TRENT, M.D., F.A.C.S., Durham, North Carolina

ON Wednesday, May 15, 1776, James Boswell, busy with his microscopic examination of the opinions, character, and behavior of the great Dr. Johnson, subjected his hero to a test.[1] He arranged for a dinner at the house of Edward and Charles Dilly, the booksellers. The other guests, not named to Johnson until he met them in Dilly's drawing room, included the radical John Wilkes, regarded by Johnson as fit only for hanging, and Arthur Lee, who, to quote Boswell, "could not but be very obnoxious to Johnson, for he was not only a *patriot* but an *American*." On being introduced into this uncongenial company, Johnson gave vent to a few resentful "tut, tut, tut's," stepped aside from the group, and fixed his attention on a book he had taken up. With the call to dinner he rejoined the others, his composure restored. Wilkes's assiduity in helping him to choice bits of veal changed composure into complacency, and Johnson was soon in a mood to enjoy fully both dinner and table talk.

Boswell's account of this momentous occasion is chiefly concerned with the conversation of Johnson, Wilkes, Lee, and himself, on such subjects as actors, poetry, and Scotland. The other guests present are mentioned only once: "Mr. (now Sir John) Miller, Dr. Lettsom, and Mr. Slater the druggist." With two of these gentlemen we are no more concerned than Boswell was, but Dr. Lettsom deserves a closer examination.

Since 1770, John Coakley Lettsom had practiced medicine in London, with notable success. A Quaker, born in the West Indies in 1744, he had been educated in a school near Lancaster, then apprenticed for five years to a surgeon and apothecary in Settle, Yorkshire. His medical education had been completed by a year in the London hospitals, and, after six months of practice in the West Indies to recruit his finances, by courses of study at Edinburgh and Leyden. He graduated M.D. at the latter university on June 20, 1769, with a thesis on tea. The young author suggests in this essay, with the authority possible only to the medical student, that the universal use of tea has been responsible, over several generations, for a noticeable decrease in the strength of the human constitution and for a consequent decrease in the frequency of violent fevers:

> "This change and diminution of inflammatory diseases, however brought about, tho' it may free us from the attacks of many violent symptoms, is nevertheless productive of more pernicious effects, and more troublesome complaints, than the former, both with respect to number & degree of violence. A multitude of Diseases, & complicated ailments have succeeded, to which our ancestors were strangers. Our Bodies have lost that strength, we admire in our ancestors, and become enervated, and liable to more diseases; and those depending upon relaxation and debility are now endemic. Hence that frequency of Hysterics in both Sexes, the Hypochondriasis, Palsy, Cachexy, Dropsy, &c.
>
> "Notwithstanding what has been advanc'd, I wou'd by no means conclude, that Tea is the sole cause of all these complaints; for luxury of every kind, to please the palate, has almost every where extended its influence, & even enter'd our Kitchens and Cellars, and contributed its share in the production of those diseases with which we labor. Under this head the frequent use of spirituous liquors stands foremost.
>
> . . . . . .
>
> "But why does this custom so frequently occur? The answer is obvious. The œconomy of the whole frame render'd weak & feeble by the constant and daily use of drinking Tea, and being sensible of debility and oppression, leads the trembling hand, to seek a temporary relief, in some cordial, in order to refresh and excite again the system. Hence such almost by necessity fall into a habit of Intemperance, and alas! Bacchus may now-a-days be represented under Petticoats."[2]

After his graduation, Lettsom visited Paris and the great spas of Europe, then returned to London, the theater of his ambitions. In 1770, he

From the Department of Surgery, Division of Thoracic Surgery, Duke University School of Medicine and Hospital.

[1] For Boswell's account of the occasion, see his Life of Samuel Johnson, LL. D., II, 82-89. London, 1791.

[2] J. C. Lettsom. Dissertatio Inauguralis Medica, sistens Observationes ad Vires Theae Pertinentes, Leyden, 1769, pp. 15-16; the English version quoted is that of a manuscript translation signed "W.C.," which is bound with the copy of the thesis in the author's collection.

John Coakley Lettsom (standing, center) is shown presenting to the Medical Society of London in 1788 the deeds of No. 3 Bolt Court, a house which was used by the Society for its meetings and library until 1850. Painted by Samuel Medley in 1800, the picture shows also Dr. James Sims, wearing a Napoleonic hat, and Dr. Edward Jenner standing at Sims's left.

married the daughter of a wealthy tin-plate manufacturer, became a licentiate of the Royal College of Physicians, and began the practice of medicine. His success in practice was almost immediate, as a result partly of the recommendation of his patron, the famous Dr. John Fothergill, partly of his own untiring efforts. He soon became one of the first physicians of London, possessed of a town residence on Basinghall Street and, ten miles away, a country estate, Grove Hill in Camberwell, where his guests could choose among the entertainments offered by an extensive library, an excellent cellar, mineralogical and numismatic collections, a botanic garden with opulent greenhouses, a complete set of apparatus for experiments in natural history, in addition to a bowling green.

Lettsom's opinion of his own profession was a curious mixture of idealism and sentiment. He aspired to be far more than a healer of the sick: he thought the physician should be a consoler of the bereaved as well, a guardian angel sent by Providence to support them in their misery; he should be a helper of the poor and a prime mover in all philanthropic endeavors; he should be not only a professional in medicine, but also an amateur of all the sciences; he should be a gentleman and a scholar, versed in history, literature—both ancient and modern—music, and the other arts. In all these directions Lettsom sought to develop himself. Medicine and humanitarian pursuits demanded most of his time; the small remainder he devoted to scientific and literary studies or to pleasant recreations with his chosen friends.

He was a prolific author, and a ready one. In his youth he was something of a poet—chiefly, it appears, on amorous subjects,—and he succumbed occasionally to the rhyming fever in later years. Most of his youthful productions have been lost; here is a sample of a mature effort:

"Far be the thought—the pleasure most sublime,
The glow of friendship, and the virtuous tear;
The tow'ring wish that scorns the bounds of time,
Chill'd in this vale of death, but languish here.

To plant the vine on Norway's wintry land,
The languid stranger feebly buds and dies;
Yet there's a clime where virtue shall expand,
With godlike strength beneath her native skies.

The lonely Shepherd on the Mountain's side,
With patience waits the rosy opening day;
The Mariner, at midnight's darksome tide,
With dreadful hope expects the morning's ray.

Thus *we*, on Life's storm-beaten ocean toss'd,
In mental vision view the happy shore,
Where *Fothergill* points to the peaceful coast,
Where Fate and Death divide true friends no more"[3]

He was also an indefatigable producer of "useful literature"—medical essays, articles on philanthropic and horticultural subjects, biographies, works on natural history. In these set pieces, his style is clear, if not always succinct; at times he attains the polished effect described in that age as "elegant." In his numerous letters, often written hastily in his carriage as he was making his professional rounds, his manner is easy and pleasant, though he occasionally wanders off into an extravagant eloquence. These letters are, by the way, full of fascinating glimpses of the scenes and personages of the day. One afternoon, for example, Lettsom slipped away from his duties to the House of Commons.

"Dundas, Pitt, Francis, Fox, North, Dempster, Scott, and many others, exhibited before me. Francis began with a two hours and half speech, with bad elocution, much specious argument, and violent party invective. Then rose young Pitt, like old Nestor: all was attention to him. There was a peculiar elegance in his attitude, a fluency and copiousness of expression; dignity in his whole manner, and great decision in his language. I felt a sensation I cannot express in seeing the Phoenix of the great Chatham at twenty-five fix every eye, and arrest submissive attention, from the most respectful Senate in the world. Fox followed him with a vehemence, a rapidity, an energy, calculated to confound rather than convert: It was more declamatory than argumentative; more violent than persuasive. I was tired before he had done, though he spoke two hours *only*. I could have listened to Pitt for ever."[4]

On another occasion, in defiance of his Quaker training, he spent an evening at the theater:

"About fourteen years ago I went to see Garrick, in King Lear, and never since have been at any theatre till the present time: it is not quite consistent with our religious system; but I confess I like to see perfection in every species of art, and this wonderful woman, Mrs. Siddons, being an object of universal admiration, I ventured, against ecclesiastical orthodoxy, to see her in Zara. . . . it is astonishing with what powers of nature and passion she can place herself in the tender movements of the heart. She speaks as if she suffered all the woe she describes; but she speaks most powerfully to the soul when she is silent: her features—her attitudes, give utterance to that language which melts the heart, and interests imagination. She is a fine figure; she is just in that medium that has softness without grossness, and tender expression without languor."[5]

This rapturous praise of Mrs. Siddons probably owed something to the vulnerability to feminine charms for which Lettsom's contemporaries occasionally criticized him.

An author himself and a diligent student of literature, Lettsom naturally found pleasure in the society of literary men. As was pointed out in the introduction of this paper, the great Dr. Johnson was among his acquaintances. There is no record of any other meeting between them than the dinner at Dilly's, but it is probable that several occurred. In any case, Johnson is the subject of much discussion in a series of letters which passed between Lettsom and Dr. William Cuming of Dorchester. The comment of contemporaries on one of the best known figures of literature, this exchange is extremely interesting. Cuming raised the subject in a letter written on May 31, 1784. After giving Lettsom the definition of the verb "to trash," Cuming remarks: "While Dr. Johnson was preparing his edition of Shakespeare's Works, I sent him this explanation of the word; but . . . he was too conceited and obstinate to adopt it."[6] Lettsom's immediate rejoinder is not known; seven months later he took occasion to write of Johnson at some length:

". . . may we . . . introduce the late Dr. Johnson, whom I suspect thou didst not fully know. He was a pious man; attached, I confess, to established system, but it was from principle. In company I neither found him austere nor dogmatical; he was certainly not polite, but he was not rude; he was familiar with suitable company; but his language in conversation was sententious; he was sometimes jocular, but you felt as if you were playing with a lion's paw. His body was large, his features strong, his face scarred and furrowed with the scrophula; he had a heavy look; but when he spoke it was like lightning out of a dark cloud. With a capaciousness of mind, and some inequalities in it, like his face, he resembled a Colossus, which, like that at Rhodes, embraced the whole sea of literature, affording awe and distance rather than esteem and social friendship: his will evinced the narrowness of his friendships; and from some of his writings, one may discern a sternness from disappointment rather than from philosophy. His Rasselas,

[3] T. J. Pettigrew. Memoirs of the Life and Writings of the Late John Coakley Lettsom. . . . With a Selection from his Correspondence. I, Correspondence, 109-110. London, 1817.
[4] Ibid., I, Corr., 62-63.
[5] Ibid., I, Corr., 72.
[6] Ibid., I, Corr., 75.

Prince of Abyssinia, was perhaps his own picture; and it inculcates apathy to the world rather than happiness in it. Upon the whole, he seems not to have been a happy man; his religion was rigid, rather than social; and his mind warped by system, rather than humanized by virtue and truth. But who is perfect?"[7]

Cuming's answer leaves no question as to his conviction of Johnson's imperfections:

"I have repeatedly read over your Character of Dr. Johnson. I shall read it again and again; the features appear to be so accurately drawn, with such a due proportion of light and shade; the praises given to his virtues and abilities so justly balanced by your candid acknowledgment of his failings and weaknesses, that I can better depend upon its being a just resemblance than on any other representation that books or conversation have ever given me of him. But yet, my friend—aye, yet—though I ever admired the great extent of his literary abilities, and few perhaps possessed greater, I could never consider him as an *amiable* character. Conscious of the superior dimensions of his own abilities, he treated others who, perhaps, were his inferiors, with a fastidious contempt. He always seemed to me . . . sententious, oracular, and dogmatical in his assertions; stiff in opinion, and hardly ever adopting that of others, however clear, in opposition to his own; narrow and illiberal in his sentiments, respecting those who differed from him in religious or political tenets, and of those who had not the felicity to be born within the jurisdiction of England. His *Dictionary*, it must be confessed, has singular merit, and exhibits a great extent of reading and judgment. . . ."[8]

Cuming completes his letter by pointing out a few flaws in the dictionary. To this barrage of criticism, Lettsom replied with an account of the dinner at Dilly's.

". . . in social company, when he unbended from critical austerity, Johnson afforded the finest dessert to a rational repast. I once dined with him, Wilkes, Boswell, and Lee the American;—what a group! 'It was ungrateful,' said Lee, 'for the Scotch, who, when emigrants, always found an asylum in America, to be the most violent opponents to American independence, and to oppose their benefactors in the cabinet and in the field.' 'The obligation,' replied Boswell, 'was not so considerable, when it is understood that the Americans sent the Scotch emigrants to Cape Fear, and such like barren regions.' 'I think,' said Johnson, 'they acted like philosophers.' 'Why?' Boswell inquired. 'Because,' added Johnson, 'if you turn a starved cow into clover, it will soon kill itself by the sudden transition; and if the Scotch, famished in their own country, had been placed in the more fruitful parts of America, they would have burst by a bellyful, like the cattle in clover.' Nobody enjoyed a laugh at the expence of the Scotch more than Boswell, at least when it came from Johnson; and the latter appeared to do it in play; but his play was as rough as that of a bear, and you felt fearful of coming within the embraces of so fierce an animal."[9]

In answer, Cuming drew an invidious comparison between the gentle and courteous manner of Dr. John Campbell, author of the *Survey of Britain*, and that of Dr. Johnson, then went on with anecdotes of his own acquaintance with the illustrious Bishop Warburton. He could not conclude without another blow at Johnson:

"Notwithstanding all that you and others have said, I must still think this said Dr. Johnson had a *feline* malevolence in his disposition, with a very narrow contracted heart, from the dislike he manifested for those who were not born in the same island. Can anything be more unworthy of a philosopher, whose mind ought to be divested of all prejudice?"[10]

At this point Lettsom seems to have abandoned the futile defense; he has no more to say about Dr. Johnson. But Cuming raised the subject again in May, 1786:

"Dr. Johnson and his biographers have employed the press, and been the subject of most conversations ever since he died. . . . That poor man's fate has been singular beyond precedent in the annals of literature. While he lived he was considered as an excellent classical scholar, as the author of several works, some of approved merit, and others of an inferior character, but known as a man of a disposition sour and *intractable;* yet still he might have been handed down to posterity as a tolerable mixt character, in some points respectable; but no sooner was the poor man laid in his grave, than four or five of his most intimate friends took it into their heads, that he merited nothing less than deification; and to work they went with a determined resolution of elevating his character beyond that of any that has ever dignified or adorned human nature. But so peculiarly unfortunate have they been in their endeavours, that every effort they made to elevate has operated in a retrograde direction, and these united efforts have dragged him down below mediocrity. His learning appears to be no ways superior to that of many others whose names have been less known. . . . His political opinions were a jargon of nonsense, his religion . . . a system of gloomy, weak, and slavish superstition. . . . His temper arrogant, contemptuous, and insolent; his disposition vain, conceited, sour, and often malevolent. Upon the whole, he was a most unamiable being; and most of these failings the intemperate and injudicious zeal of his best friends has by a strange fatality brought to light . . . Boswell's and Piozzi's works are wonderfully trifling and inconsistent. . . . I am sorry to hear that Boswell is deaf to every remonstrance, and fear that this affair will end fatally for his intellects."[11]

The biographers suffer even more severely in a letter which Cuming wrote on June 6, 1787. He has been reading Sir John Hawkins' life of Johnson, and finds that the hero "loses ground in (his) estimation, by every page that (he) peruse(s), and that Johnson's whole life seems to be a great aggregate of inconsistency, want of judgment, strong prejudices, gloomy superstition, supreme arrogance, and gross rudeness of manners."[12] And the biographers have brought all this to light:

"His character may be compared to Cæsar's mangled robe, when displayed by Marc Antony to the Roman people, after the assassination:—'Look! in this place ran Piozzi's (Cassius) dagger! through this the well-beloved Boswell (Brutus) stabbed! See! what a rent the envious Hawkins

[7] Ibid., I, Corr., 77-78.
[8] Ibid., I, Corr., 82-83.
[9] Ibid., I, Corr., 84-85.
[10] Ibid., I, Corr., 91-92.
[11] Ibid., I, Corr., 115-117.
[12] Ibid., I, Corr., 124.

(Casca) made.' And he is still doomed to further indignities by the publication of his Life threatened by Boswell."[13]

It is not recorded that Lettsom came to the defense of Boswell, a fact which seems surprising when it is remembered that the biographer was a closer friend of his than ever Johnson was. They had probably met long before the Johnson-Wilkes dinner, at one of the frequent parties that gathered at the Dilly house during the early seventies, and they must have met often during Boswell's many stays in London thereafter. Both men were present at a dinner given by Charles Dilly on October 23, 1787, when Boswell "was very low, and injudiciously had recourse to too much wine to raise (his) spirits."[14] They met again at Dilly's on May 9, 1790 and on July 29, when Boswell again "drank rather too liberally."[15] John Nichols informs us that on occasions when Charles Dilly found it necessary to leave his guests earlier than he wished, he deputed "the pleasure of entertaining them" to Boswell, "who sometimes, in that capacity, has tried the strength of *the oldest binn*."[16] Whether or not Lettsom was ever present on such an occasion, he had ample opportunity to observe Boswell's convivial indulgences, for on June 18, 1791, he found it desirable to address to his Scottish friend a serious warning.

"When I acknowledge that ever since I had the pleasure of thy acquaintance I have felt a singular esteem for thee, I only express a sentiment which every other person must feel if placed in the same situation. The generosity, the candour, the openness of thy heart, combine to acquire and to secure the attachment of every liberal mind. This attachment I presume to claim; it is this that compels me to risk thy future friendship, by embracing the freedom which it inspires.

"I have, my friend, had some occasion of viewing thee in the most interesting situations, when thy whole soul has been poured out in social enjoyment, I might have said extacy, and in no point of view canst thou appear more endearing; for those will love thee most who see most of thy heart. But in these scenes of pleasure, which I have cordially enjoyed, sometimes a sigh of solicitude has burst upon me, lest by any unguarded excitement of such conviviality a bodily constitution may be undermined, and that life thereby shortened, which every man of refinement and virtuous sociality must wish long, very long preserved.

"I have observed, not merely a too frequent use of the glass, but that mixture of liquors which, as a professional man, I can add, tends to injure the best human fabrick. I will add further, what ample experience authorizes, that by whatever means the spirits are exhilarated beyond the chaste medium of nature, the alternation of mental languor will result; so that the depression is great in proportion to the degree of foreign excitement.

"Two motives embolden me thus to recall sober reflection. to chasten and to moderate the fascinating influence of social pleasures, either too frequently repeated or too far extended. I feel in the first place the emotions of friendship, which I cannot repress; and in the next, the intrinsic solid sense of one I am proud to call my friend: these equally impel me to risk his censure, whilst the latter encourages me to subscribe myself his sincerely,

J. C. Lettsom."[17]

This letter Boswell apparently took in good part, as he had taken similar advice from Johnson years before. He did not, of course, pay much heed to Lettsom's warning; in a letter to Lettsom written six months later, he partly explains his state of depression by admitting that he has not followed Lettsom's "friendly recommendations as to regimen. *Spero meliora*."[18] Certainly Lettsom took no measures to remove temptation from his friend's way; Boswell dined with him on November 6, 1793, and describes the evening thus:

"At Dr. Lettsom's was a numerous Company, several of those whom I had seen at his house in Camberwell. We sat late and drank a great deal of wine. Sir John Peter, late Consul at Ostend, carried me in a coach with his Lady to their lodgings in Liecester Square, and made me go up and take a glass of liqueur; and then was so kind as to proceed with me in the coach to my own door and see me safely at home, I being a good deal intoxicated."[19]

Boswell made one of the party at Grove Hill on several occasions; his journal contains a pleasant record of one visit on August 21, 1790:

"Mr. Dilly and I dined with Dr. Letsom at his charming villa at Camberwell Grove. A Mr. ——, an old gentleman of Aberdeen who had lived long at Santa Cruz and had been 36 years without being in Britain, dined there, as did Dr. Sims, the irish City Physician. We played at bowls both before and after dinner, two gentlemen of Camberwell, whose names I forget, having joined us. I relished the amusement much, and was conscious of being carried along the stream of life with no steady direction but without positive pain, for which I am so framed as to think I may compound."[20]

The joys of the villa are more fully and fairly presented in an "Horatian Ode to Charles Dilly," which Boswell composed in honor of Grove Hill and its master:

"My cordial Friend, still prompt to lend
Your cash when I have need on't;
We both must bear our load of care—
At least we talk and read on't.

Yet are we gay in ev'ry way,
Not minding where the joke lie;
On Saturday at bowls we play,
At Camberwell with COAKLEY.

[13] Ibid., I, Corr., 124-125.
[14] Private Papers of James Boswell from Malahide Castle, XVII, 49. Privately printed, 1931.
[15] Ibid., XVIII, 33, 83.
[16] John Nichols. Literary Anecdotes of the Eighteenth Century, III, 192, n. London, 1812-1815.
[17] Pettigrew, op. cit., II, 384-385.
[18] Ibid., II, 386.
[19] Private Papers of James Boswell, XVIII, 225.
[20] Ibid., XVIII, 90.

Methinks you laugh to hear but half
The name of Dr. LETTSOM:
From him of good—talk, liquors, food,—
His guests will always get some.

And guest has he, in ev'ry degree,
Of decent estimation;
His liberal mind holds all mankind
As an extended Nation.

. . . .

LETTSOM we view a Quaker true,
'Tis clear he's so in one sense:
His *Spirit*, strong, and ever young,
Refutes pert PRIESTLEY'S nonsense.

In Fossils he is deep, we see,
Nor knows Beasts, Fishes, Birds ill:
With Plants not few, some from Pellew,
And wondrous *Mangel-Wurzel!*

West India bred, warm heart, cool head,
The City's first Physician:
By schemes *humane*, Want, Sickness, Pain,
To aid is his ambition.

From terrace high he feasts his eye,
When practice grants a furlough;
And, while it roves o'er Dulwich groves,
Looks down—ev'n upon THURLOW!"[21]

Fortunately Lettsom's literary acquaintance included one who was a better poet than Boswell, though his name is now nearly forgotten. John Scott of Amwell, the Quaker poet who won Dr. Johnson's difficult affections, was long Lettsom's friend and apparently his literary adviser as well.[22] Scott's verses on Grove Hill take up with Boswell's closing note—the striking view, 150 miles in circumference, which the site of Grove Hill afforded—then Scott turns to Lettsom himself:

"That business with fatiguing cares
For this delightful seat of thine
Such scanty store of moments spares,
Say, friend, shall I for thee repine?
Were it the commerce of the main,
Or culture of the teeming plain,
From blame or pity I should scarce refrain.

But, oh, to alleviate human woes,
To banish Sickness, banish Pain;
To give the sleepless eye repose,
The nerveless arm its strength to gain;
From Parents' eyes to dry the tear,
The Wife's distrestful thought to chear,
And end the Husband and the Lover's fear;

Where Want sits pining, faint and ill,
To lend thy kind unpurchas'd aid,
And hear the exertions of thy skill
With many a grateful blessing paid;—
'Tis luxury to the feeling heart,
Beyond what social hours impart,
Or Nature's bounteous scenes, or curious works of Art."[23]

[21] John Nichols. Illustrations of the Literary History of the Eighteenth Century, II, 664-665 n. London, 1817 1858.
[22] Pettigrew, op. cit., II, 325-326.
[23] John Scott, "Eulogy on Grove-Hill," Gentleman's Magazine, LXV (August, 1795), 685.

The estate was celebrated in still another set of verses by the oriental scholar and historian, Thomas Maurice. A clergyman, Maurice was a voluminous writer and one of the first to popularize the knowledge of the history and religions of the East. He wrote and published many poems, one of which Lord Byron scathingly described as "the petrifactions of a plodding brain." His rapturous poem on Grove Hill first describes Lettsom the physician, then Lettsom the botanist:

"Not only man's frail race thy skill befriends,
To vegetable life thy skill extends . . . ."[24]

A tour of the Grove Hill botanic garden, library, and museum follows, couched in the peculiarly maddening roundabout diction so popular with the worst eighteenth-century poets. The account of the library has some interest beyond its style:

". . . . Science there has fix'd her favourite seat,
There cherish'd Genius finds a safe retreat!
There, honour'd and renown'd through ev'ry age,
The mighty fathers of the classic page,
Who wak'd, in Greece or Rome, the soul of song,
Or roll'd the tide of eloquence along;
Assembled in their deathless works appear,
And seem to charm again the ravish'd ear;
There too each great and venerated name,
Enroll'd upon the page of modern fame;
Sages, whose daring minds have nobly soar'd,
And wide the spacious vault of Heav'n explor'd;
Or, darting downward, pierc'd the central gloom,
Where burning gems the boundless shade illume,
And mark'd great Nature, in the secret mine,
With chemic pow'r the glowing ore refine;
Patriots, who, proudly prodigal of blood,
The rage of fiercest tyrants have withstood;
And statesmen, of unspotted honour prov'd,
By freedom cherish'd and by Britons lov'd;
An awful throng! in sculptur'd marble frown,
And fire the soul to deeds of high renown."[25]

A few words on that library at Grove Hill will not be out of place, and will serve to clarify the stilted phrases of Mr. Maurice. It was a splendid collection, ample in scope, but particularly rich in medical and natural history. The many pieces of value included an unpublished letter of Hippocrates, once the possession of Askew. Lettsom acquired it at a sale for ten shillings and sixpence, his agent, Dr. Sims, having let the other bidders know by whom it was wanted.[26] Another notable curiosity was a seven-volume work by Jacob Christine Schaffers, in which the leaves of the volumes were formed of vegetable and other substances. The classics were represented in a collection of choice editions, gathered by the printer

[24] Thomas Maurice. "To John Coakley Lettsom, M. D., on the Improvements at his Villa of Grove-Hill," Gentleman's Magazine, LXV (August, 1795) 686.
[25] Ibid., p. 686
[26] Pettigrew, op. cit., I, 122-123.

William Baker and purchased by Lettsom after Baker's death.

The library bookcases were divided into sixteen compartments, each topped by a bust of some personage appropriate to the subjects of the books beneath him.[27] Thus John Wesley presided over Tracts and Miscellanies; Addison over Reviews; Pott over Surgery and Chemistry; Stukeley over Antiquities and Medals; Hogarth over Prints and Maps. Newton topped Arts and Sciences; Locke, Divinity and Law; Bacon, Dictionaries and Classics; Voltaire, History and Biography; Milton, Poetry; Raleigh, Voyages and Geography; Boyle and Franklin, Natural History; Sydenham, Medicine; Fothergill, Medicine and Botany; Mead, Hortus Siccus and manuscripts.

Lettsom found it necessary to dispose of Grove Hill some years before his death, and a part of his library, which was too large for his town residence, had also to be sold. It was auctioned off by Leigh and Sotheby, during the week of March 26, 1811. At his death in 1814, Lettsom still possessed a library of over 12,000 volumes, which was sold by the same dealers two years later.[28]

Lettsom's many other literary acquaintances can be mentioned only briefly. He was for decades the friend and physician of John Nichols, editor of the *Gentleman's Magazine*, who described Lettsom as one who gladdened as well as lengthened life. Charles Dilly, the bookseller, was Lettsom's publisher and devoted friend throughout their mature lives, and at his hospitable table Lettsom met authors and scholars by the score. On his death Dilly left the physician a legacy of five hundred pounds. Lettsom's varied interests brought him the acquaintance of many philanthropists including John Howard and John Nield, of the botanist William Curtis, the naturalist Peter Collinson, the mythologist Jacob Bryant. He corresponded widely with men of letters and science in other countries, with Rush, Franklin, and Waterhouse in America, Zimmermann in Hanover, and William Thornton in the West Indies—the last-named was designer not only of the Capitol building at Washington but also of a universal alphabet calculated to solve all linguistic difficulties.

Lettsom held yet another place in the literary history of his time: he was always a generous and helpful patron to men of letters. As Pettigrew writes: "In him the sons of genius were sure to find a friend."[29] One of the writers who owed much to Lettsom's aid has been mentioned—William Curtis, the botanist. A result of Lettsom's awareness of the general neediness of the writing clan appears among his philanthropic essays, a paper entitled "Hints for Establishing a Society for Promoting Useful Literature."[30] The proposed society would give rewards, pecuniary or honorary, to deserving authors, would establish prizes, care for the widows and orphans of authors, and erect monuments to deceased genius. This "hint" of Lettsom's is of particular interest, for, while itself ineffectual, it preceded by ten years the establishment of the Literary Fund.

Many institutions of learning, also, owe a debt to Lettsom. From his American friends in particular, he received many appeals on behalf of colleges and libraries. Dr. Rush wrote for Dickinson College in 1785:

> "I know the pleasure you take in doing good; I know your zeal in promoting knowledge; and hundreds testify to your partiality to the American States. Will you give me leave to solicit your friendship to our College, in begging a few books from your friends for our library? the sweepings of their studies will be very acceptable in our illiterate wooden country. The lumber of the stalls in the streets of London, which are sold by weight, would make us truly rich."[31]

Waterhouse sponsored Harvard; James Bowdoin presented the needs of the college named after his father. To each Lettsom sent liberal donations. In 1890 the managers of the Pennsylvania Hospital asked Lettsom's aid in purchasing books for their library; he not only supplied much useful advice, but also sent volumes from his own library.[32]

John Coakley Lettsom was convinced of the fact that the physician should be "a gentleman and a scholar, versed in history, literature, music and the other arts," and shaped his life accordingly. Today in our struggle for the mastery of science, particularly as it applies to our special fields, we as physicians too often neglect the humanities, become narrow and limited in our ideas and fail to assume that leadership in cultural pursuits which is our heritage. Certainly Lettsom, one of the greatest physicians of the eighteenth century, as a cordial friend of literary men and a generous patron of learned institutions also earned a place, however small, in the annals of literature.

[27] Ibid., I, 165-166.
[28] Nichols. Illustrations of the Literary History of the Eighteenth Century, II, 665,n.
[29] Pettigrew, op. cit., I, 147.
[30] First published in the Gentleman's Magazine, April, 1780.
[31] Pettigrew, op. cit., II, 427.
[32] Catalogue of the Medical Library of the Pennsylvania Hospital, Philadelphia, 1829, pp.vii-viii.

REVIEWS OF NEW BOOKS

THE book *A Textbook of Gynaecological Surgery*[1] is one that all gynecologists and surgeons should have in their library. It is both interesting and advantageous to have available a book which presents the English point of view and methods so excellently. The radical abdominal operation (Wertheim) for carcinoma of the cervix is thoroughly discussed. These authors have had a tremendous experience with this procedure. Their thinking on the subject is set forth clearly and all aspects are discussed. The current arguments concerning subtotal and total hysterectomies and vaginal versus abdominal hysterectomies are considered and their opinions are given.

Their conservative attitude toward removal of the ovaries is to be commended and their statements are well worth reading.

The chapters on "Remote Results of Gynaecological Operations" and "Postoperative Complications" are extremely interesting.

The dangers inherent in the performance of each surgical procedure are listed and discussed. This makes the book a handy reference.

The infusion and transfusion procedures differ quite widely from those carried out in America. On the basis of scientific knowledge our practices seem more fundamentally sound.

While the changes and additions in this edition are not numerous, the complete thoroughness of the book makes it valuable. JOHN I. BREWER.

THE volume entitled *A History of the Heart and Circulation*[2] by Dr. Willius and Dr. Dry follows the general principle that history is composed of biographies. Thus, throughout the work page after page introduces a new character usually with his portrait and an interesting statement of his contribution. In the first part of the book this biographical material is grouped into chronological epochs ending with the first quarter of the twentieth century. Then a very interesting series of special biographies is presented beginning with Hippocrates and ending with modern authorities such as Wenckebach, Mackenzie, Osler, and Lewis.

There is in conclusion, a section presented according to subjects such as arrhythmia, intracardiac circulation, surgery of the heart and blood vessels, and so forth. Each chapter and division is accompanied by numerous references so that the volume, although relatively small, is a starting point for any extensive and thorough review.

One may therefore urge that this book on the history of the heart be read for interest and education, and that it may also be used as an important secondary source. PAUL STARR.

THE second edition of *Intracranial Tumors*[3] is a classical discussion of intracranial neoplasms, written by Percival Bailey, a distinguished neuropathologist and neurosurgeon. It continues the tradition of the first edition published in 1933. Very few changes in content are readily apparent, perhaps indicating the stagnation of neurosurgical effort in the control or understanding of neoplastic growth during these 15 intervening years. The author states that the main thesis of the volume remains unchanged, but errors have been corrected and recent advances in knowledge inserted. Sixteen plates depicting gross changes in the x-ray study of the skull, brain, and cerebral vascular system during tumor development have been appended to the text. Only 32 of the 521 references represent material published since 1941.

The method of presentation of an admittedly difficult subject should be uniquely valuable to the student of neurology. The text may be described as a refined and readable version of lectures presented to students. It may be read with profit by any specialist in this field since it reveals one expression of neuropathological thought in a certain time period that may shortly be of historical interest alone.

The volume opens with a short discussion of the problem of tumors in general, followed by two chapters devoted to the structure of the cranium and the elements of neurophysiology. Thirteen discrete cerebral tumors or tumors involving specific tissues, such as connective tissue, are then presented in separate chapters and are worthwhile reading for the student indeed. Each tumor or group of tumors is identified by brief historical notes. Several case reports are then detailed, followed by a discussion of the gross and microscopic structure of the neoplasm. These pathologic features are illustrated by black and white drawings that do not fairly represent the author's vast knowledge of this phase of neurosurgery. Even if the microscopical drawings are intelligible to the student, they must at least discourage any further pursuit of the subject.

The main substance of each chapter is found in the author's often lengthy, but always lucid, discussion of clinical neurological syndromes. These may be considered as superb lessons in neuroanatomy, neurophysiology, and neurology, pointed and

[1] A TEXTBOOK OF GYNAECOLOGICAL SURGERY. By Victor Bonney, M.S., M.D., B.Sc. (Lond.), F.R.C.S. (Eng.), Hon. F.R.A.C.S., Hon. F.R.C.O.G., M.R.C.P. (Lond.)., and Sir Comyns Berkeley, M.A., M.C., M.D. (Cantab.), F.R.C.P. (Lond.), F.R.C.S. (Eng.), M.M.S.A. (Hon.), F.R.C.O.G. 5th ed. New York: Paul B. Hoeber, Inc., 1948.

[2] A HISTORY OF THE HEART AND THE CIRCULATION. By Fredrick A. Willius, M.D., M.S. in Med., and Thomas J. Dry, M.A., M.B., Ch.B., M.S. in Med. Philadelphia & London: W. B. Saunders Co., 1948.

[3] INTRACRANIAL TUMORS. By Percival Bailey. 2nd ed. Springfield: Charles C. Thomas, 1948.

enlivened by the preceding case histories and the neuropathological data. These are "sharply defined syndromes characteristic of the various pathological types of tumors in different locations in the intracranial cavity" and nowhere in neurological literature have they been better presented.

The eighteenth chapter has to do with the matter of general diagnosis. It is marked by the sound, but often disregarded, advice to the young physician to learn to use the ophthalmoscope as well as he does the stethoscope, by the author's adversion to the use of ventriculography, and by failure to mention electroencephalography as a valuable adjunct in tumor diagnosis. The next chapter touches upon the various facets of differential diagnosis, a large subject in itself, which the author presents in an effort to stimulate the student in his ancillary reading. More modern references, such as those of Ingraham in subdural hematoma in infants and those of Dandy in congenital cerebral aneurysm, for instance, would aid in this worthwhile project.

The twentieth, and last chapter, recounts the author's principles of treatment of intracranial tumors. Few neurosurgeons agree with one another in terms of neurosurgical technique, but there will be some who will dispute any use of intracapsular removal of acoustic neurinomas or the advice to disregard the temporal intradural approach to pituitary tumors. Some neurosurgeons will use oxygen instead of air for ventriculography and will mention intratracheal ether as a good anesthetic agent. They will be happy to use the electrocautery in bleeding from brain tissue, and gelatin sponge and hemostatic synthetic bone wax and tantalum clips, and begin craniotomies with a transfusion rather than end them with such resuscitation methods.

In spite of these minor differences of opinion, and the use of fourth decade techniques, their results will be little different from those that are graphically and dispassionately revealed by the author. In this book the great contribution to brain surgery of neurology and tissue pathology are brilliantly disclosed by a master in these fields. Some part of the technical achievements of neurosurgery is at most suggested. The appalling impasse in which the surgery of cerebral gliomas now finds itself is all too obvious. The hope for the future does not lie "in the direction of increasing our knowledge and acumen so that we can foretell before operation—the nature of the tumor to be attacked as well as its location." This hope has been in large part achieved. This volume can act as a standard springboard into unchartered waters, whatever they may be, but its philosophy of thought can produce nothing more. BARNES WOODHALL.

THE monograph *Osteosynthesis with a Long Intramedullary Metal Pin (Küntscher's Method)*[1] by Emile Jan Möeys although not as elaborate as some other presentations, notably Böhler's, does add definitely to the literature on medullary nailing and is a work which can be read with profit by everyone interested in fractures. To some extent the method has been accepted in this country for the treatment of certain shaft fractures, and the opinion of a surgeon like Möeys who reports after an experience with over 250 cases must be considered as definitely authoritative. Möeys believes that "this method is a great advance in the field of fracture surgery" and even one with little or no experience with the medullary nail must agree with him after studying his essay.

The work discusses briefly at first the object of all fracture treatment and then gives more in detail the "essentials of the method" with separate headings for: (a) reaction of the bone marrow, (b) possibility of fat embolism, (c) chance of infection, (d) general reaction to the presence of the metal pin, and (e) influence of the pin on callus formation. Apparently although there are definite temporary changes in the blood picture after introduction of a nail and sometimes until it is removed, no harmful effects have ever been seen and the possibility of fat embolism is no greater than in fractures treated by other methods. Möeys goes into the subjects of the reaction of bone to metal, as well as fracture and callus formation at some length. The chapter on the latter subject is well worth reading. He sums up by stating the use of the nail is "ideal both in anatomical and functional respect" and mentions that Böhler reduced the hospital stay in certain types of femoral fractures from between 240 to 340 days to 45 days with the Küntscher pin. The second half of the monograph gives an excellent but short review of the literature and then discusses in detail the technique of the method as applied by the author. A special table is used and a roentgenologist is always present to guide the nail by means of the fluoroscope and the use of so-called "wringers," which are like large Thomas wrenches, to control the fragments. In open fractures this help is of course unnecessary as the guide wires are introduced at the site of the fracture. Möeys states that the most important thing is reduction of the fracture and that by using his "specially constructed table we succeeded in all cases. Then the operation itself is a minor procedure."

Details of 100 cases are given which add to the size of the volume but which add very little to the knowledge of the reader and can be skipped if desired. The bibliography is apparently very complete and can be used by anyone interested not only in the Küntscher method but in fracture healing in general.

The monograph should be available to all surgeons working in large, well organized clinics where the method can be applied, but it probably will not be of any practical interest to the average doctor as yet. WALLACE H. COLE.

IN *The Mechanism of Abdominal Pain*[2] by V. J. Kinsella, clinical investigations of abdominal pain

[1] OSTEOSYNTHESIS WITH A LONG INTRAMEDULLARY METAL PIN (Küntscher's Method). By Emile Jan Möeys. Utrecht: Kemink en Zoon N.V., 1948.

[2] THE MECHANISM OF ABDOMINAL PAIN. By V. J. Kinsella, M.B., Ch.M. (Syd.), F.R.C.S. (Eng.), F.R.A.C.S. Sydney: Australasian Medical Publishing Co., Ltd., 1948.

are reported and an extensive bibliography is reviewed. Attention is called to the misconception concerning the absence of afferent fibers in the sympathetic nervous system. The author concludes that a belief in true visceral pain has an adequate anatomical basis and presents reasons for believing that direct visceral tenderness occurs. No sharp dividing line was found between sensitive and insensitive regions in the abdomen. A neurohumeral basis to replace the neuronal basis for abdominal pain is postulated. The effective stimulus for pain is raised tension within the tissues, due to inflammatory reaction, or to powerful muscular contraction, or both. Tenderness in visceral disease is believed primarily and essentially to be that of the diseased visceral tissue; parietal tissues may be secondarily involved. Rigidity is believed probably due to a simple spinal reflex. The varieties of abdominal pain are recorded and the attempt is made to understand them upon the simple basis of direct visceral sensibility.

WALTER H. NADLER.

THE little volume *Anatomia funcional del sistema nervioso Vegetativo*[1] by Prieto and Uria approaches the neurovegetative system from a purely functional viewpoint. It is believed that to separate function from morphology is a mistake, particularly inasmuch as no significantly new neuromorphologic contribution has been broached in recent times. The book is a compendium of a larger work in preparation on nervous functional anatomy. It presents the important features which have come to light recently, and gives a résumé of modern thought on the matter.

Interpretation of the morphologic function of the vegetative nervous system has undergone numerous modifications, the fault of garbled nomenclature. The first chapter attempts to unravel this situation. Afterward such topics as the functional systematization of nuclei associated with peripheral nerves, functional localization of the hypothalamus, cranial parasympathetics, metasympathetics, innervation of the circulatory apparatus and other organs are considered in orderly chapters. The book concludes with an appreciation of vegetative sensibility, and numerous unusually clear contrast illustrations make the volume a worthwhile acquisition, particularly for the beginning student of neurology.

STEPHEN A. ZIEMAN.

THE book *Chirurgie modern de la hanche; appart de la radiographie de profil*[2] by René Charry was not intended to be a comprehensive treatise on hip conditions. The author describes some of the more common arthropathies and their surgical treatment. Vitallium cup arthroplasty is not mentioned and hip fusions are not discussed. Great emphasis is placed on the lateral x-ray view of the hip, using the Judet-Mathieu technique, which apparently is similar to that commonly used in this country under the name of Manfredi. The author points out the x-ray findings in different positions of rotation and stresses the fact that the posterior articular margins of the hip in the lateral view are parallel. He discusses congenital dislocation of the hip as seen in the adult, and he distinguishes between subluxation and luxation. In the former, osteoarthritis is the rule and invariably develops after the age of 35. On the contrary, true luxation does not develop arthritic changes unless treatment was attempted in early childhood. The author supports his view with observations made in operative cases. In subluxation, the lateral x-ray view reveals that the posterior articular margins are not parallel and the femoral head is slightly displaced anteriorly. When this is recognized early, an "anterior buttress" graft is indicated. The operation is technically difficult but is has the advantage of preventing the development of arthritic changes. When osteoarthritis has already supervened, an arthroplasty is the treatment of choice. The author employs fascia lata to cover the femoral head; vitallium cup arthroplasty is not mentioned.

The author continues with the description of other forms of osteoarthritis and atrophic arthritis pointing out that in these conditions the posterior articular margins of the hip are parallel in the lateral x-ray view. He discusses the various operative procedures of neurectomy, drilling and pegging, shelf stabilization, osteotomies, Mathieu's resection arthroplasty with their indication and their relative value. The latter procedure (which apparently is very similar if not identical with the Whitman operation) is preferred to hip fusion.

In cases of old luxation of the hip the author describes the accepted operative procedures (shelf stabilization, osteotomy), but in limited cases he prefers to do an open reduction, resecting an inverted V-shaped segment of bone through the trochanteric region and transplanting the greater trochanter to the shaft of the femur. However, since no end-results and other statistical data are mentioned, this procedure cannot be properly evaluated.

In coxa vara, the lateral view shows slight anterior displacement of the head. The author performs an "anterior buttress" graft and transplants the greater trochanter on the shaft. His results are excellent; however, again, no statistical data are furnished.

Although the book is entitled *Modern Surgery of the Hip*, the reader will not find in it such commonly accepted procedures as vitallium cup arthroplasty and Brittain's arthrodesis. Apparently this was beyond the scope of the book. The text is well illustrated with 512 roentgenograms and tracings and makes interesting reading. C. L. JEANNOPOULOS.

THE author of *Venous Thrombosis and Pulmonary Embolism*[3] by Harold Neuhof has been interested in the subject for many years. This monograph is

[1] ANATOMIA FUNCIONAL DEL SISTEMA NERVIOSO VEGETATIVO. By Ramon Lopez Prieto and Francisco Garcia Uria. Valladolid: Tipografia Cuesta, 1947.

[2] CHIRURGIE MODERNE DE LA HANCHE. Apport de la Radiographie de Profil. By René Charry. Paris: Gaston Doin & Cie Editeurs, 1948.

[3] VENOUS THROMBOSIS AND PULMONARY EMBOLISM. By Harold Neuhof, M.D. New York: Grune & Stratton, 1948.

based on a study of 88 fatal pulmonary emboli observed in an 11 year period at the Mount Sinai Hospital in New York between 1927 and 1938. All cases have been verified by autopsy and excellent diagrams are used to illustrate the site and extent of pulmonary emboli. There is a critical review of the literature, and a new approach for the extraction of pulmonary emboli is described, which, while unsuccessful in this particular case, certainly merits further study and development. This method was first published in 1944 and no other report has followed this attempt.

Obviously, the first part of the book was written later than the second; it contains a large number of histories with critical comments and illustrates the changing concepts in the author's mind toward more anticoagulant therapy. While in a controversial field as this lack of agreement is not unusual and invites further progress, one must point to certain discrepancies between the author's statements.

Thus for instance, while he is convinced that major pulmonary emboli, with the exception of a cardiac source, came overwhelmingly from the legs, he presents histories which show that lower abdominal pain (a pelvic thrombus) preceded the closure of the iliofemoral segment. He does not take much stock in the reflex effects of pulmonary emboli and yet describes two perfect examples of minor pulmonary emboli with a patent main pulmonary artery, both of which were fatal with symptoms of a shock-like state. He does not mention the increased tendency to clotting as an important factor in thromboembolic phenomena and yet describes cases in which propagating thrombosis occurred in the contralateral extremity under the customary dosage of heparin. One has the feeling that there is too much reference to part 2 in part 1 of the volume and that logically the first part, written later, should follow and not precede the second one.

With these minor exceptions, however, the great merits of this monograph should be stressed. The author advocates an extensive search for iliac thrombi, free or adherent after sectioning the common femoral vein; he states that there is no dependable relationship between the location and extent of the pulmonary embolus and the clinical symptoms; he veers more and more to anticoagulant therapy in calf-muscle thrombosis and does not believe in ligation of the superficial femoral vein.

The monograph is of interest to all general surgeons as it is a true account of the problems confronting them in their daily practice. Many questions, of course, remain unsettled, but it is through publications of this sort that an agreement can be reached as to the simple and safe measures to prevent and treat pulmonary embolism. While the presentation is repetitious, this is a provocative book, which should be in every surgeon's library. Most refreshingly a detailed study of individual histories is presented in contrast to mass statistics, which often have the musty order of record libraries and seldom add diagnostic refinements.

GEZA DE TAKATS.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

PREGNANCY DIAGNOSIS TESTS: A Review. By Alfred T. Cowie, B. Sc., M.R.C.V.S., Ph. D. Published by the Commonwealth Bureaux of Animal Breeding and Genetics, Edinburgh: Dairy Science, Shinfield; Animal Health, Weybridge, 1948.

ABDOMINAL OPERATIONS. By Rodney Maingot, F.R.C.S. (Eng.) 2nd ed. New York: Appleton-Century-Crofts, Inc., 1948.

THE RH BLOOD GROUPS AND THEIR CLINICAL EFFECTS. By P. L. Mollison, A. E. Mourant, and R. R. Race. London: His Majesty's Stationery Office, 1948.

MANUAL OF UROLOGY. By R. M. LeComte, M.D., F.A.C.S. 4th ed. Baltimore: The Williams & Wilkins Co., 1948.

ELEMENTARY ANESTHESIA. By W. N. Kemp, M.D., C.M. Baltimore: The Williams & Wilkins Co., 1948.

AMERICAN MEDICAL ASSOCIATION INTERNS' MANUAL. Philadelphia and London: W. B. Saunders Co., 1948.

TECHNIC OF MEDICATION. By Austin Smith, M.D., C. M., M. Sc. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1948.

TEXTBOOK OF ANAESTHETICS. By R. J. Minnitt, M.D. (Liverpool), D. A. (R. C. P. & S. Eng.), and John Gillies, M.D., M.B., Ch. B. (Edin.), F.R.C.S. (Edin.), D.A. (Eng.) 7th ed. Baltimore: The Williams & Wilkins Co., 1948.

REPRODUCTION AND SURVIVAL. By R. Christie Brown, M.B., M.S., F.R.C.S., F.R.C.O.G. London: Edward Arnold and Co., 1948.

AN INTRODUCTION TO SURGERY. By Rutherford Morison, M.D., F.R.C.S. (Edin.), F.R.C.S. (Eng.), M.A., D.C.L., LL.D., and Charles F. M. Saint, C.B.E., M.D., M.S., F.R.C.S., F.R.A.C.S. 4th ed. Baltimore: The Williams & Wilkins Co., 1948.

THE SURGERY OF ABDOMINAL HERNIA. By George B. Mair, M.D., F.R.F.P.S.G., F.R.C.S.E. Baltimore: The Williams & Wilkins Co., 1948.

ACUTE INTESTINAL OBSTRUCTION. By Rodney Smith, M.S., F.R.C.S. With a chapter on radiological diagnosis by Eric Samuel, M.D., F.R.C.S., F.F.R., D.M.R.E. Foreword by Rupert Vaughan Hudson, F.R.C.S. Baltimore: The Williams and Wilkins Co., 1948.

BACTERIAL AND MYCOTIC INFECTIONS OF MAN. Edited by René J. Dubos, Ph. D. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1948.

THE PRACTITIONER TEXTBOOKS. The Practice of Endocrinology. Edited by Raymond Greene, M.A., D.M., M.R. C.P. London: Eyre & Spottiswoode Ltd., 1948

EDUCATION FOR PROFESSIONAL RESPONSIBILITY. Pittsburgh: Carnegie Press, 1948.